

**MYOFASCIAL RELEASE AS A  
TREATMENT CHOICE FOR  
NEUROMUSCULAR CONDITIONS: THREE  
RANDOMISED CONTROLLED TRIALS  
AND A SYSTEMATIC LITERATURE  
REVIEW**

**A thesis submitted in partial fulfilment of the requirements of the  
University of Bolton for the degree of Doctor of Philosophy on the basis of  
published work**

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**May 2018**

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**Doctor of Philosophy**

**(PWP Route-A Retrospective)**

**University of Bolton, Bolton, UK, 2018**

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# Abstract

**Introduction:** Myofascial release (MFR) is a form of manual therapy that involves the application of a low load, long duration stretch to the myofascial complex, intended to restore optimal length, decrease pain, and improve function. MFR is being used to treat patients with a wide variety of conditions, but there is a scarcity of evidence to support its efficacy. Studies are emerging in this field with varying results and conclusions. Analysis of the recent research trials and reviews will be a better way to appraise the quality and reliability of such works.

**Objective:** This work attempts to analyse and summarise the evidence from three randomised controlled trials (RCTs) and one systematic review of the effectiveness of MFR on various neuromuscular conditions and pain.

**Methodology:** Effectiveness of MFR on tension type headache, lateral epicondylitis and chronic low back pain were the RCTs identified for the analysis. The systematic review selected analysed the published RCTs on MFR till 2014. The methodological qualities of the studies were assessed using the PEDro, Centre for Evidence-Based Medicine's (CEBM) Level of Evidence Scale, Risk of Bias (RoB) Analysis Tool and AMSTAR 2.

**Results:** The RCTs analysed in this study were of moderate to high methodological quality (PEDro scale), with higher level of evidence (CEBM scale) and less bias (RoB). The effectiveness of MFR on tension type headache (TTH) was the first among the studies with a moderate methodological quality (6/10 in PEDro), with a 2b level of evidence on the CEBM scale. The study proved that direct technique or indirect technique MFR was more effective

than the control intervention for TTH. The second RCT studied MFR for lateral epicondylitis (LE). The study was of a moderately high quality on the PEDro scale (7/10) with a 1b- level in CEBM. The MFR was found more effective than a control intervention for LE in computer professionals. The RCT on chronic low back pain (CLBP) also scored 7/10 in the PEDro scale and 1b in the CEBM scale. This study confirmed that MFR is a useful adjunct to specific back exercises and more helpful than a control intervention for CLBP. All three RCTs stated the usage of self-report measures and underpowered sample size as the major limitations along with a performance bias reported in the TTH trial.

The systematic review demonstrated moderate methodological quality as per the AMSTAR 2 tool which analysed 19 RCTs for a result. The literature regarding the effectiveness of MFR was mixed in both quality and results. Omission of a risk of bias analysis was the major limitation of this review. The authors quoted that “MFR may be useful as either a unique therapy or as an adjunct therapy to other established therapies for a variety of conditions”.

**Conclusion:** Critical appraisal is an important element of evidence-based medicine to carefully and systematically examine research to judge its trustworthiness, its value and relevance in a particular context. This review concludes that the three RCTs and the systematic review analysed were completed with moderate to good quality as per various quality measures, but with reported methodological flaws and interpretation biases. These studies with the critical appraisal can act as ‘pavements’ on which high quality future MFR trials and evidence can be built on.

**KEY WORDS:** *myofascial release, myofascial release therapy*

## List of Published Works

1. **Ajimsha, M. S.**, 2011. Effectiveness of direct vs indirect technique myofascial release in the management of tension-type headache. *Journal of Bodywork and Movement Therapies*, 15(4), 431-435.
2. **Ajimsha, M. S.**, Chithra, S., & Thulasyammal, R. P., 2012. Effectiveness of myofascial release in the management of lateral epicondylitis in computer professionals. *Archives of Physical Medicine and Rehabilitation*, 93(4), 604-609.
3. **Ajimsha, M. S.**, Daniel, B., & Chithra, S., 2014. Effectiveness of Myofascial release in the management of chronic low back pain in nursing professionals. *Journal of Bodywork and Movement Therapies*, 18(2), 273-281.
4. **Ajimsha, M. S.**, Al-Mudahka, N. R., & Al-Madzhar, J. A., 2015. Effectiveness of myofascial release: Systematic review of randomized controlled trials. *Journal of Bodywork and Movement Therapies*, 19(1), 102-112.



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M.S. Ajimsha

# Statement of Original Authorship

The work contained in this thesis has not been previously submitted for a degree or diploma at any other higher education institutions to the best of my knowledge and belief. This thesis is structured based on the regulations and procedures governing the award of the degree of 'Doctor of Philosophy by Published Work' by University of Bolton, UK.



M.S. Ajimsha

May 2018

## **Dedication**

I would like to dedicate this thesis to my wife, Chithra. S, without her help and motivation this doctoral research would not have been a success. I would like to remember my little kid Juan Ren for his cheerful smile and understanding during the tougher periods of my thesis writing. To my mother (late) 'Mamma I miss you'.

## List of Abbreviations

MPS	Myofascial Pain Syndrome
NSAID	Non-Steroidal Anti-Inflammatory Drugs
TrPs	Trigger Points
LTR	Local Twitch Response
MFR	Myofascial Release
PT	Physical Therapy
FRC	Fascia Research Congresses
RCT	Randomised Controlled Trial
PEDro	Physiotherapy Evidence Database
CEBM	Centre for Evidence-Based Medicine
RoB	Risk of Bias Analysis
PNF	Proprioceptive Neuromuscular Facilitation
TTH	Tension-Type Headache
DT-MFR	Direct Technique Myofascial Release
IDT-MFR	Indirect Technique Myofascial Release
SD	Standard Deviation
MFTRF	Myofascial Therapy and Research Foundation
M/F	Male/Female
N	Number
H	Hour
vs	Versus
LE	Lateral Epicondylitis

CLE	Chronic Lateral Epicondylitis
PRTEE	Patient-Rated Tennis Elbow Evaluation
ANOVA	Analysis of Variance
SALBP	Subacute Low Back Pain
CLBP	Chronic Low Back Pain
SBE	Specific Back Exercises
MPQ	McGill Pain Questionnaire
QBPDS	Quebec Back Pain Disability Scale
SMFR	Sham Myofascial Release
SUST	Sham Ultra Sound Therapy
SLR	Straight Leg Raise
US	Ultrasound
NP	Neck Pain
TMD	Temporo Mandibular Disorder
IMT	Intra-oral MFR Therapy
ROM	Range of Motion
BCS	Breast Cancer Survivors
RT	Reaction Time
ECM	Extracellular Matrix
5-HT	5-Hydroxytryptamine
FICAT	Federative International Committee on Anatomical Terminology
DNA	Deoxyribonucleic Acid
N	Newton
CNS	Central Nervous System

a-SMA	Alpha Smooth-Muscle Actin
HRMT	Human Resting Myofascial Tone
mRNA	Messenger Ribonucleic Acid
IGF	Insulin Growth Factors
MGF	Mechano-Growth Factors
GH	Growth Hormone
TGF-b	Transforming Growth Factor Beta
PDGF	Platelet Derived Growth Factor
TLF	Thoracolumbar Fascia
LD	Latissimus Dorsi
G Max	Gluteus Maximus
IL	Interleukin
GTO	Golgi Tendon Organ
PRO	Patient Rated Outcome
PROM	Patient Rated Outcome Measures
EE	Estimate of Effect



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# Chapter 1

## Introduction

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*1.1. Introduction*

*1.2. Fascia Explained*

*1.3. Biomechanics of Fascia*

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# Chapter 1

## Introduction

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### 1.1. Introduction

Musculoskeletal pain and dysfunction are amongst the leading reasons for visits to physicians and manual therapists and are the most common cause of long-term chronic pain, affecting people worldwide in the range of hundreds of millions (Woolf & Pfleger, 2003). Without proper treatments, chronic pain can have a strong disruptive impact on an individual's physical, psychological and social well-being. At the societal level, pain creates a tremendous economic and workplace burden. As the prevalence of musculoskeletal pain is projected to rise with a sedentary but longer living worldwide population (Woolf & Pfleger, 2003), it calls for greater effort in the development and evaluation of new ways of managing these patients. Recent studies have demonstrated the role of fascia in various musculoskeletal dysfunctions as the fascial tissues connect the skeletal muscles forming a body wide web with some pattern called as 'myofascial meridians' (Luomala & Pihlman, 2016). As fascia is able to modify its tensional state, strain transmission along the meridians might occur in response to changes of muscle activity (Wilke et al., 2016).

Fascia is a ubiquitous tissue permeating the entire body. It surrounds, supports, suspends, protects, connects and divides muscular, skeletal and visceral components of the organism (Kumka & Bonar, 2012). It not only lubricates the fibres but gives nourishment to all parts of the body (Still, 1910). The fascial system is considered as a "tensegrity" or tensional

integrity structure to manage the balance between tension and compression around the organs, joints and muscles (Chen et al., 2016). Its continuity aids in force transmission both longitudinally and epimuscularly (Maas & Sandercock, 2010; Yucesoy, 2010). Through ‘mechanotransduction’, these forces may be transmitted at a cellular level, altering gene expression of fibroblasts and thereby changing the extracellular matrix composition (Langevin et al., 2010; Chaitow, 2016).

Repetitive mechanical straining of fibroblasts can also result in secretion of inflammatory mediators (Dodd et al., 2006). All of these changes could affect the normal functions of force transmission or sliding in the musculoskeletal system. This dysfunction could lead to pain or proprioceptive issues, considering that fascia has been shown to be innervated. Thus, treatment of disorders affecting the musculoskeletal system may need to be focused on this fascial network (Kwong & Findley, 2014). Recently, treatments of fascial tissues have become increasingly popular in musculoskeletal disorders (Wilke et al., 2016).

This tensional network of fibrous tissues includes dense sheets such as muscle envelopes, aponeuroses, as well as specific local adaptations, such as ligaments or tendons (Schleip et al., 2013). The importance of the fascia to normal function has been recognized by ‘hands-on’ practitioners for more than a century (Still, 1910; Findley & Shalwala, 2013) but it is only recently that it has emerged as a significant contributor to mainstream orthopaedic knowledge (Schleip et al., 2012).

There are multiple theories as to how myofascial tissue is altered after trauma or overuse, extending from cellular (viscoelasticity, piezoelectricity, tensegrity etc.) to global level (force transmission, sliding, fluid dynamics, hysteresis, innervation, sensitisation etc.), which are explained later in this thesis. Chronic tension in fascia, impaired fascial healing response, damage to proprioception, alteration of collagen fibre composition, transformation

of fibroblasts into myofibroblasts, or changes in ground substance were the most attributable pathological processes mentioned in literatures (Liptan, 2010; Stecco et al., 2010).

After an injury, inflammation may occur, which could have a role in altering fascia. The biochemical milieu of myofascial trigger points- hyperirritable spots in the fascia surrounding skeletal muscle- has been shown to contain many substances both locally and remotely, including substance P, calcitonin, gene-related peptide, bradykinin, 5-hydroxytryptamine, norepinephrine, tumor necrosis factor alpha, and interleukin 1-beta (Kwong & Findley, 2014). These inflammatory substances may result in activation of fibroblasts into myofibroblasts when combined with a tensioned environment (Tomasek et al., 2002). This, in turn, may lead to alterations in gene expression (Arnsdorf et al., 2010) causing changes in the extracellular matrix including altered ‘hyaluronic acid’ production. This may result in restriction in fascia, leading to altered lines of force with muscle contraction (Stecco et al., 2013; Meltzer et al., 2010). These processes may contribute to the decreased movement between fascial layers (Langevin et al., 2011). Over time, these biomechanical changes from restricted fascia could lead to decreased strength, coordination, (Ercole et al., 2010; Stecco et al., 2013) pain or proprioceptive issues; considering that fascia has been shown to be innervated (Tesarz et al., 2011). Thus, treatment of disorders affecting the musculoskeletal system may need to be focused on this fascial network.

Studying fascia objectively at the basic science and clinical levels will provide important information that may change clinical practice. Once the structure and functions of fascia in the musculoskeletal system are further elucidated, the pathophysiology of many disorders and their consequences may be better explained. Many neuromuscular and musculoskeletal disorders can be additionally served by research with a fascial perspective in order to optimize treatment strategies (Kwong & Findley, 2014).

## 1.2. Fascia Explained

Once dismissed as a packing tissue of little consequence, the fascia is now recognized as a continuous interconnected network that permeates and envelops almost every part of the body and is now taking its rightful place at the ‘top table’ of anatomical and physiological research (Scarr, 2016). Fascia is an uninterrupted viscoelastic tissue which forms a functional three-dimensional collagen matrix (Kumka & Bonar, 2012; LeMoon, 2008) “continuous throughout the entire organ” (Purslow & Delage, 2012) with many diverse and important functional roles (Schleip et al., 2012a; Tozzi, 2015a). “Fascia is the place to look for the cause of disease and the place to consult and begin the action of remedies in all diseases” (Still, 1899).

The term ‘fascia’ refers to dense planar tissue sheets such as the ‘deep’ or ‘investing’ fascia (fascia profunda), septa, aponeuroses, joint and organ capsules, the epimysium that surrounds muscles, the softer ‘superficial’ fascia beneath the skin, the intra-muscular endomysium that surrounds individual muscle fibres and perimysium that surrounds bundles of these fibres. It also includes the dura mater, periosteum, neurovascular sheaths, abdominal mesentery etc. and is continuous with ‘non- fascial’ densifications in the form of ligaments, tendons (Benjamin, 2009; Schleip et al., 2012b), periosteum and bone (Aaron, 2012). Because fascia has a sheet-like structure attaching to muscles and bones at multiple sites, it is exposed to different states of multi- or biaxial strain.

Fascia surrounds, supports, suspends, protects, connects and divides muscular, skeletal and visceral components of the organism (Kumka & Bonar, 2012; Schleip, 2003). It is formed of numerous layers of collagen fibre bundles (Stecco et al., 2007a) and is extremely strong (Findley et al., 2012) but plastic (Schleip, 2003). It has been reported that fascia displays piezoelectric effects (Façade & Yasuda, 1964), alters in stiffness following changes in water content (Chaitow, 2009), is richly innervated with nerve endings (Benjamin, 2009; Stecco et al., 2007a) and contains many mechanoreceptors (Yahia et al., 1992).

Fascia seems to be integrally involved in the biomechanics of the musculoskeletal system (Gerlach & Lierse, 1990), may be involved in force transmission (Benjamin, 2009), may contract like smooth muscle (Schleip et al., 2005), and can become inflamed and potentially cause pain (Bednar et al., 1995).

The fascia plays different physiological and functional roles related to joint stability, general movement coordination, proprioception, nociception (Tozzi, 2012) and is associated with wound healing, tissue repair and many connective tissue pathologies (Gabbiani, 2003). Fascia is a continuous structure that attaches, stabilizes, encloses and separates almost all internal organs including muscles and bones. The fascia embodies the element of structural interconnectedness around, within and between body elements starting from the cellular level, with simultaneous sliding and gliding motions (Tozzi, 2015a). Since it appears everywhere in the body with its characteristics structure and functions, it has been referred to as both an ‘organ of form’ (Varela and Frenk, 1987) and as an ‘organ of innerness’ (“due to its phenomenological dimension of ‘in between’ the ‘outer’ and the ‘inner’ boundaries of the body”) (Tozzi, 2015a). Instead of consisting of different superimposed layers, gliding on each other, it has been proposed as a single architecture with various levels of form and complexity (Guimbertau, 2012). It has been defined as an ‘ectoskeleton’ (Wood Jones, 1944), in relation to its continuity and function of muscle attachment, enveloping, force transmission and body-wide proprioception.

Even at a cellular level, fascia displays an interconnected arrangement with soft tissue fibroblasts within the Extra-cellular matrix (ECM) forming an extensive reticular network, via their cytoplasmic expansions, that permeates the whole body (Langevin et al., 2004). Fibroblasts may actually form ‘adherens’ and ‘gap junctions’ at the intercellular levels of contact, allowing also for a more concerted response to mechanical loading (Ko et al., 2000). Furthermore, each fibroblast’s cytoskeleton is structurally connected to the external



environment, either directly with contiguous cells or through the ECM constituents (Fletcher & Mullins, 2010). The entirety of this system may indeed represent a body-wide signalling network (Langevin, 2006) that depends on the relationship between cells and the surrounding matrix. Mechanical tension signals from the ECM are transferred through transmembrane mechanoreceptors to the cytoskeleton and cell nuclei, while being transduced into chemical information -via mechanotransduction- so impacting on various aspects of cell behaviour and metabolism via the modulation of gene expression (Wang et al., 2009; Tozzi, 2015a).

The myofascia is a fibrous specialization of fascial/ ECM tissues that enclose and interpenetrate muscles as a complex hierarchy of tubes containing smaller tubes within them; and is continuous with higher-level fascial tubes that surround groups of muscles, the limbs and entire body (Scarr, 2016). Bundles of collagen fibres within the perimysium and epimysium are typically aligned in two distinct directions that together form crossed-helical patterns, and this arrangement also appears within the deep investing fascia surrounding groups of muscles and the body wall (Tozzi, 2015b). These particular fibre orientations are a reflection of the most efficient distribution of mechanical stresses; and the same basic principles are likely to apply to the walls of all these tubular sheaths (Tozzi, 2015b).

### **1.2.1. Fascial Classification System**

In an effort to organize nomenclature for fascia provided by the ‘Federative International Committee on Anatomical Terminology’ (FICAT), Kumka, & Bonar (2012) developed a functional classification system which includes four categories of fascia: i) linking, ii) fascicular, iii) compression and iv) separating fasciae.

### **1.2.1. a. Linking Fascia**

The linking category is predominantly dense, regular, parallel ordered and unidirectional connective tissue proper with a significant amount of collagen type I (Gordon & Hahn, 2010). This includes fasciae of muscles, fasciae of regions (head & neck, trunk, limbs), aponeuroses, tendinous arches and neurovascular sheaths (FICAT, 2008).

This category is subdivided into dynamic and passive divisions (Kumka, & Bonar, 2012). The dynamic division includes major fascial groups more significantly related to movement and joint stability, and characterized by higher concentrations of contractile and proprioceptive fibres. The dynamic division is composed of fasciae of muscles (investing layer, fascia of individual muscle) and fasciae of the trunk (FICAT, 2008).

The passive division is acted on by other extramuscular tissues to maintain continuity throughout the body or form tunnels and sheaths (van der Wal, 2009). The passive division incorporates fasciae of muscles (muscle sheaths), fasciae of the head and neck, fasciae of limbs, aponeuroses, tendinous arches, and retinaculae (Kumka, & Bonar, 2012). The passive linking fasciae can only transmit force when they are stretched and loaded, while dynamic fasciae can theoretically contract more autonomously like smooth muscle, thereby affecting tension in the musculoskeletal system, but not significant enough to be the primary mover of limbs (Schleip et al., 2005).

### **1.2.1. b. Fascicular Fascia**

Fascicular fascia forms adaptable tunnels which bundle vessels as well as fascicles within muscle, tendon, bone and nerves. Fascicular fascia plays an important role in organization, transport, strength and locomotion (Purslow & Delage, 2012). This category is organized as a mixture of both loose and dense regular multidirectional connective tissues (FICAT, 2008). Types I and III collagen are the major components of these tissues with lesser

amounts of Types V, VI, XII, and XIV (Gordon & Hahn, 2010; Purslow & Delage, 2012). Fascicular fascia of the muscle comprises three distinct layers: epimysium, perimysium and endomysium (Purslow & Delage, 2012).

The fascicular fascia of the muscle converges into a dense, regular connective tissue link at the myotendinous junction to become fascicular fascia of the tendon, comprising endotendon, peritendon and epitendon (van der Wal, 2009). At this junction, fascicular fascia is richly innervated by Golgi tendon organs which are stimulated by muscle contraction (Ross & Pawlina, 2011). Tension in the tendon results in a reflex decrease in tonus in contiguous striated muscle fibres (Langevin & Sherman, 2007).

Fascicular fasciae allow forces to be transferred from within muscle to synergistic muscles, and also, via the extramuscular pathway, through the linking fascia, to antagonistic muscles (Huijing, 2009). The fascicular fascia forms the connective tissue envelope for nerve fascicles and whole peripheral nerves: perineurium and epineurium, respectively (Ross & Pawlina, 2011). The perineurium serves as a metabolically active diffusion barrier that contributes to the formation of a blood-nerve barrier (Passerieux et al., 2006).

### **1.2.1. c. Compression Fascia**

Compression fascia is a mixture of dense regular woven and multidirectional parallel ordered connective tissue layers that ensheath the whole limbs to create a stocking effect (FICAT, 2008). This fascial category plays an important role in locomotion and venous return due to its influence on compartmental pressure, muscle contraction and force distribution (Stecco et al., 2009). The spatial orientation of the collagen fibres changes from layer to layer within the compression fascia. The presence of loose connective tissue interposed between adjacent layers permits local sliding, allowing the single layers to respond more effectively (Stecco et al., 2009).

### **1.2.1. d. Separating Fascia**

Separating fascia is generally loose connective tissue and dense irregular fusocellular connective tissue (FICAT, 2008). The reticular Type III collagen fibres and elastic fibres are the major components of the ECM of separating fascia, with small amounts of collagen Types V and VII. While the reticular fibres provide a supporting framework for the cellular constituents, the elastic fibres form a three dimensional network to allow separating fascia to respond to stretch and distention (Ross & Pawlina, 2011). Separating fascia divides the body in visible sheets and layers of varying fibres allowing it to take up forces and friction in all directions. While its major function is to allow more efficient sliding of tissues over one another, it may still form adhesions from faulty movement patterns or injury (Hedley, 2010).

FICAT's terms for separating fascia include: parietal fascia, visceral fascia, extraserosal fascia and investing/subcutaneous fascia. This category also includes synovial sheaths and fasciae of limbs (FICAT, 2008). Parietal fascia lies outside the parietal layer of serosa such as pericardium, pleura and peritoneum and lines the wall of a body cavity. Visceral fascia lies immediately outside the visceral layer of the serosa and surrounds the viscera. Extraserosal fascia lies within the space between the visceral and parietal fasciae (FICAT 2008).

This fascia class is a complex connective tissue matrix, enveloping everything from body cavities to individual organs. It separates, supports, and compartmentalizes organs and regions in order to maintain proper structural and functional relationships throughout the body. This group of fascia has a unique appearance and texture upon observation, ranging from transparent woven sheets to a fuzzy cotton-like consistency (Hedley, 2010).

### 1.2.2. Histology

Fascia has specific cells, ground substance and fibre types that make it a form of connective tissue proper (Kumka, & Bonar, 2012). Collagen, a triple helix glycoprotein, is the key structural fibre that gives connective tissue its ability to resist tension. There are twenty five distinct collagen types recognized in the Ross histology textbook and atlas, and twenty eight collagen types recognized in the latest review by Gordon (Ross & Pawlina, 2011; Gordon & Hahn, 2010). Although, type I collagen is the main type accounting for 90% of the human body's collagen, fascia contains an array of collagen type combinations including, but not limited to, types I, III, IV, V, VI, XI, XII, XIV and XXI (Gordon & Hahn, 2010). Collagen provides resistance to tension and stretch, which commonly occur in fascial tissues, such as ligaments, tendons, sheaths, muscular fascia and deeper fascial sub-layers (Ross & Pawlina, 2011).

Collagen type III, also known as reticular fibre, is involved in forming the scaffolding for the cells of the loose connective tissues related to the endoneurium, vascular walls and smooth muscle (LeMoon, 2008). A collagen fibril needs the support of not only fibrillar collagen types, but also a mix of non-fibrillar forms known as fibril-associated collagens with interrupted triple helices (FACITs). The functions of FACITs include: i) anchoring to the basement membrane, ii) regulating the diameter of fibrils, iii) forming lattice networks and iv) acting as transmembrane structures (Gordon & Hahn, 2010). These fibrils are important to the integrity and function of fascia within the ECM. Elastic fibres within the ground substance give fascia its characteristic stretch (Kumka, & Bonar, 2012).

A combination of multiple types of collagen within the extracellular matrix forms a unique structure, like a blueprint that reflects the function and compliance of fascia in various regions. Without a characteristic fibre arrangement and composition for each fascial region, it

is likely that fascia would not withstand stresses or have the same function (Kumka, & Bonar, 2012).

The cells within fascia include fibrocytes (fibroblasts, myofibroblasts), adipocytes and various migrating white blood cells (Chirasatitsin & Engler, 2010). Fibroblasts are highly adaptable to their environment and show a capacity to remodel in response to the direction of various mechanical stimuli, producing biochemical responses (Stecco et al., 2009; Meltzer et al., 2010). If function changes, as with increased mechanical stress, or prolonged immobilization, deoxyribonucleic acid (DNA) transcription of pro-collagen in the fibroblasts will change types (e.g., collagen type I into collagen type III), or undifferentiated cell types may adapt towards a more functionally appropriate lineage (e.g., chondrocyte) (Kumka, & Bonar, 2012).

It was established that the tissue structure and the molecular composition of ECM are directly correlated with the local mechanical forces. Under significant states of compression, tissue once populated with fibroblasts becomes invested predominately with chondrocytes and forms specialized connective tissue, cartilage, with further solid mineral deposition (Milz et al., 2005). These adaptations have been demonstrated in the supraspinatus tendon, transverse acetabular ligament, transverse ligament of atlas, as well as various other ligaments and tendons throughout the body (Milz et al., 2005).

Myofibroblasts within fascia demonstrate contractile properties and contain actin-myosin filaments typically seen in smooth muscle. An estimation of tension created by contraction of myofibroblasts when extrapolated to a large fascial sheet (i.e., thoracolumbar fascia) may produce tension within the musculoskeletal system between 30–40N (Schleip et al., 2009).

Increased concentration of myofibroblasts in pathological fascia has been observed, suspected to create tissue contractures in clinical conditions like palmar fascial fibromatosis (Dupuytren's disease), plantar fascial fibromatosis (Ledderhose's disease) and adhesive capsulitis (frozen shoulder) (Hedley,2010). Fascia is also susceptible to the actions of typical cells of inflammation influencing communication, growth and function (Ross & Pawlina, 2011).

Based on certain common characteristics, including the fibre arrangement, connective tissue proper is classified by the Terminologia Histologica as loose connective tissue and dense connective tissue. The dense connective tissue is sub-categorized as: i) unidirectional parallel ordered dense connective tissue, ii) multidirectional parallel ordered dense connective tissue, iii) woven connective tissue and iv) irregular fusocellular connective tissue (Kumka, & Bonar, 2012).

### **1.2.3. The Helical Tube**

The myofascia, as a fibrous specialization of fascial/ECM tissues that surround and interpenetrate muscles is then a complex hierarchy of helically-reinforced tubes contained within larger tubes and continuous with higher-level fascial tubes that surround groups of muscles, the limbs and entire body. Bundles of collagen fibres within the perimysium and epimysium form crossed-helical configurations that balance longitudinal and circumferential stresses and coordinate changes in muscle shape during contraction and extension and should thus be considered as an essential part of muscle function (Scarr, 2016). Tendon has a hierarchical structure that links tendon, fascicle, fibre and fibrils. In particular, tendon fibres are made up of fibrils that have distinctive wavy forms called crimps (Shim et al., 2012).

The 'walls' of the perimysium and epimysium are distinct in that they frequently contain two crossed-ply sets of collagen cables aligned at about 55-60° (relative to the long

axis in resting fusiform muscles). All these angles increase with muscle contraction and when the muscle is stretched the angles decrease (Chaudhry et al., 2012).

The cross helical model of fascial fibre arrangement are indeed contributing to the coordination of changes in muscle shape. They would also enable such tubes to bend smoothly without kinking and resist torsional deformations, thus further demonstrating the value of this particular arrangement to muscle mechanics (Scarr, 2016). Biological helixes consist of multiple discrete components (fibres) arranged into these particular geometric configurations since they are the most efficient packing arrangement within a dynamic environment (Pickett et al., 2000).

Myofibroblasts generate significant tensional forces due to the presence of smooth muscle-like actin filaments within their cytoskeletons and transfer this into the surrounding ECM through transmembrane proteins, and they play an important role in tissue contracture during wound healing and other fascial pathologies (Tomasek et al., 2002). This contractile ability thus enables myofibroblasts to contribute to the intrinsic tension/passive stiffness of muscle and other tissues (Schleip et al., 2006), and perhaps even assist in organizing or fine-tuning the crossed-helical lattice as the most efficient distribution of tension.

#### **1.2.4. Fascial Remodelling**

Fascia, when regularly put under increasing yet physiological strain, the inherent fibroblasts adjust their matrix remodelling activity such that the tissue architecture better meets demand. Fascial tissues also react to their dominant loading patterns. With the help of the fibroblasts, they slowly but constantly react to everyday strain as well as to specific training, steadily remodelling the arrangement of their collagenous fibre network (Kjaer et al., 2009).

Research has confirmed the previously optimistic assumption that proper exercise loading -if applied regularly- can induce a more youthful collagen architecture, which shows a



more wavy fibre arrangement (Jarniven et al., 2002) and which also expresses a significant increased elastic storage capacity (Schleip & Müller, 2013)

### **1.2.5. Myofascial Meridians**

Muscles of the human body do not function as independent units. Instead, they are regarded as part of a tensegrity-like body-wide network, with fascial structures acting as linking components (Wilke et al., 2016). Myofascial Meridians are based on gross anatomy and the ability of the myofascial system to pull, transmit strain, rebound, facilitate movement and provide stability to the human body (Tozzi, 2015a). Myers (2009, 2014) defined eleven myofascial meridians connecting distant parts of the body by means of muscles and fascial tissues. The central rule for the selection of a meridian's components is a direct linear connection between two muscles. The theory of the myofascial meridians helps manual and movement practitioners explore how one structure affects other distance structures in the body. Because fascia can transmit tension (Norton-Old et al., 2013) and in view of its proprioceptive and nociceptive functions, existence of myofascial meridians could be responsible for disorders and pain radiating to remote anatomic structures (Myers, 2009).

The myofascial meridians have been referenced in several studies (Hyong & Kang, 2013; Weisman et al., 2014; Grieve et al., 2015). Despite the references, the theory of the myofascial meridians is based on anecdotal evidence rather than evidence based research. Wilke et al. (2016), first showed that there was good evidence for the existence of three myofascial chains proposed by Myers (2009, 2014) through a systematic review, a search for peer-reviewed anatomic dissection studies published from 1900-2014. The review was adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The methodological quality of the enclosed studies was evaluated by using QUACS scale (QUality Appraisal for Cadaveric Studies) by two independent evaluators. Of these studies, evidence of each meridian and its transitions were classified as strong, moderate,

limited, conflicting or not existent (Wilke et al., 2016). A transition was considered a myofascial link between two muscles. For example, the gastrocnemius and hamstring are considered to be a transition of the superficial back line. The results yielded strong evidence for myofascial transitions in three of the six examined myofascial meridians: Superficial back line, back functional line and front functional line. In the superficial back line, three myofascial transitions (plantar fascia-gastrocnemius, gastrocnemius-hamstrings and hamstrings-lumbar fascia/erector spine) were verified in fifteen studies. In the back functional line, three myofascial transitions (latissimus-lumbar fascia, lumbar fascia-gluteus maximus and gluteus maximus-vastus lateralis) were verified in eight studies. Finally, the front functional line verified strong evidence for two myofascial transitions (pectoralis major-rectus abdominis and rectus abdominis-adductor longus) in six studies. There was moderate evidence for the meridians and transitions of the spiral line (five of nine verified transitions, based on twenty one studies) and the lateral line (two of five verified transitions, based on ten studies). There was no evidence for the meridians and transitions of the superficial front line, based on seven studies) (Wilke et al., 2016).

The practical relevance of the findings by Wilke et al. (2016) regarding the existence of myofascial meridians can help explain how lines of pull and compensations in one structure of the body can impact other distance structures. As a result, more appropriate diagnostic, therapeutic and exercise strategies can be developed by manual and movement practitioners for their patients and clients.

The research by Wilke et al. (2016) is the first systematic review to provide solid evidence for the existence of the ‘anatomy trains’ or myofascial meridians, especially for the superficial back line and front and back functional lines. Most of the reviewed studies did not specifically search for the finding of facial connectivity but mentioning them as a subordinate finding. Future studies can address and rectify these limitations. Future studies should include

randomised controlled in-vitro studies since most of the experimental researches were carried out using cadavers (Norton-Old, 2013; Barker et al., 2004). It will also be valuable to conduct further research on the spiral, lateral and superficial front lines to determine if there is stronger evidence to support their existence and begin to explore evidence for the deep front line and arm lines. Overall the finding from this systematic review can be considered as a starting point for further high-quality studies in search of the existence of strain transmissions across tissues connected by myofascial meridians.

Therapists may use the myofascial chains as a conclusive orientation, but they should be aware that the functional implications remain to be studied (Wilke et al., 2016). Currently an increasing number of clinicians and anatomists show continued interest in the subject of myofascia, hence the possibility of further researches focused on the existence of myofascial links remains very high (van der Wal, 2009). The existence of myofascial meridians might help to explain the phenomenon of referred pain, which often occurs in nonspecific disorders. For example, myofascial trigger points of the calf have been shown to elicit pain that radiates to the sole of the foot and the dorsal thigh (Travell & Simons, 1992).

Direct morphologic continuity between adjacent muscles provides the empirical background to extend diagnostic and therapeutic focus beyond a single anatomic structure (Wilke et al., 2016). Treatment according to myofascial meridians could be effective in reducing low back pain. Several studies have shown that patients with low back pain display reduced hamstring flexibility (Feldman, 2001; Hultman et al., 1992). Due to the direct morphologic relation of the hamstrings and low back region (both are part of the superficial back line) relieving tension of the posterior thigh muscles could be a conceivable approach to alleviate pain. Overload injuries in competitive sports represent another entity of pathologies which possibly occur because of the presence of myofascial meridians (Wilke et al., 2016).

Labovitz et al. (2011) and Bolivar et al. (2013) indicate that tightness of the gastrocnemius and hamstrings is associated with plantar fasciitis (PF). Since gastrocnemius, hamstring and the plantar aponeurosis belong to the superficial back line, they might represent a target of exercise therapy. The study by Labovitz et al (2011) was a prospective cohort study with an aim of finding if hamstring tightness was an increased risk in PF and found that patients with Hamstring tightness were about 8.7 times as likely to experience PF in the corresponding foot compared with patients without hamstring tightness. Bolivar et al., in 2013, has tested almost the same hypothesis with 100 subjects in a case control study and proved that tightness of the posterior muscles of the lower limb was significantly correlating with the incidence of PF. Both the studies suggested that a stretching protocol for treatment of PF should look for both hamstring and triceps surae tightness. Since both studies were in non-randomised format, caution is needed in interpreting the findings and its generalisability. It also necessitates high quality confirmation studies to ascertain these findings.

A study by Wilke et al., in 2015 evaluates the remote effects of lower limb stretching on cervical range of motion (ROM) based on the myofascial meridians and found that lower extremity stretching induced improvements of cervical range of motion and proved the existence of strain transfer along the course of myofascial meridians. This was a pilot study with a matched-pairs comparison. These findings have to be verified by using randomised, controlled studies with adequate sample size. The authors also pointed towards the limitations in the outcome measure used as it could not identify whether increases in flexibility were attained in flexion, pointing towards a measurement bias.

In the later part of the year 2016, Krause et al., conducted a systematic review on intermuscular force transmission along myofascial chains based on cadaveric studies and in-vivo experiments. This systematic review concluded that the tension/force can be transferred between at least some of the investigated adjacent myofascial structures. Even though the study

is concluding positively, the authors quoted that the applicability of the current results to in-vivo conditions was hampered by three factors (i) heterogeneity in methods of force application, (ii) variation in the assessed outcomes and methods between studies and examined body regions and (iii) factor relates to the use of cadaver specimen for biomechanical testing (Krause et al., 2016). It is also crucial to consider anatomical variations in continuity as well as histological differences in the linking structures when interpreting results. The study conducted by Krause et al. thus gives more in-depth analysis of the possible pitfalls in the current researches on the myofascial meridians existence. This study ends up by suggesting that such experiments should be done on fresh cadavers, as fixation as well as freezing and thawing could alter its biomechanical properties. The study concluded that future studies on the in-vivo behaviour of adjacent structures should further investigate the practical relevance of the proposed intermuscular myofascial connections for exercise prescription, injury prevention and rehabilitation.

Wilke et al., in 2017(a) conducted a medium quality (PEDro Scale: 6/10, CEBM: 2b) randomised controlled study on sixty three healthy participants to compare the effectiveness of remote stretching based on myofascial chains as with local exercise on cervical range of motion (ROM). The participants were randomly assigned to one of three groups: remote stretching of the lower limb (LLS), local stretching of the cervical spine (CSS) or inactive control (CON). Prior (M1), immediately post (M2) and five minutes following intervention (M3) maximal cervical ROM were assessed. Both LLS and CSS increased cervical ROM compared to the control group in all movement planes and at all measurements ( $P < .05$ ). Between LLS and CSS, no statistical differences were found ( $P > .05$ ). The study concluded that lower limb stretching based on myofascial chains induces similar acute improvements in cervical ROM as local exercise. Methodological flaws and inadequate power hinders the study's generalisability.

The authors have given caution in interpretation as “attained effects do not seem to be direction-specific, further research is warranted in order to provide evidence-based recommendations”.

Although these reviews yield positive evidence for the existence of myofascial chains and myofascial force transmissions, several aspects need further clarifications and in depth analysis. Future research should be dedicated to the presence of the meridians and force transmissions which could not be evidenced entirely in these works. Another issue related to the function of regional specializations so far remains unclear. Depending on its localization, fascia in general exhibits substantial differences concerning thickness, amount of elastic fibres (Stecco et al., 2008) and adherence and expansions to the surrounding soft tissues including muscles (Stecco et al., 2009). Also, the number of connecting fibres are not uniform and shows considerable variation for different transitions (Snow et al., 1995). This holds particular significance as the structures linking the muscular stations of the meridians encompass tendinous, aponeurotic and ligamentous tissue as well as the deep fascia. Finally, it is of utmost importance to elucidate the functional significance of the myofascial chains as the capability for strain transfer represents the decisive criterion to justify treatment of meridians. Randomised controlled in-vivo studies are warranted in order to draw more precise assumptions on the significance of myofascial chains for the movement system. Therapists may use the myofascial chains as a conclusive orientation but should be aware that the functional implications remain to be studied (Wilke et al., 2016).

### **1.3. Biomechanics of Fascia**

The importance of the fascia to normal function has been recognized by ‘hands-on’ practitioners for more than a century (Still, 1899; Findley & Shalwala, 2013). But it is only recently that it has emerged as a significant contributor to mainstream medical knowledge (Schleip et al., 2012). It appears that the fascia mediates an active mechanical transference role

as it provides dynamic connections between and among the muscles and bones (Yang et al., 2015).

Passive myofascial tension, independent of CNS control, furnishes a basic stabilizing component to aid and maintain a balanced posture (Lunghi et al., 2016). This refers to a skeleton of soft tissue for muscular insertions called ‘ectoskeleton’. Moreover, the phenomenon of neurogenic inflammation triggered by stimulation of nociceptive receptors (Deising et al., 2012) in fascia tissues is consistent with the notion that disruption of fascia physiology can have notable consequences on human health.

Fascia is also capable of transmitting electrical signals throughout the body (Findley & Shalwala, 2013). Collagen, which is one of the main components of fascia, has been shown to have semiconductive, piezoelectric and photoconductive properties in-vitro (Yang et al., 2015).

### **1.3.1. Fascia-Related Mechanisms Associated to Somatic Dysfunction**

#### **1.3.1. a. Fasciogenic Model**

The Fasciogenic model of somatic dysfunction (Tozzi, 2015a) emphasizes two main interacting fascial changes - structural and functional - that may underlie somatic dysfunction and account for its palpable features (tissue texture changes, asymmetry, restriction of motion and tenderness). Several dysfunctional events may produce different forms of forces and responses in the fascia with consequent dysfunctional processes.

Zink & Lawson (1979) proposed that myofascial compensation pivots on four anatomical ‘transitional areas’ (lumbopelvic, thoracolumbar, cervicothoracic and craniocervical) that play a major role not only in defining the spinal curves, but also in compensating regional patterns, both during the periods of development and learning but also in adult life. (Lunghi, 2015).

### ***1.3.1. b. Fascial Architecture***

Fibroblasts display cytoskeletal remodelling as part of normal function and, in particular, under changes in mechanical tension, resulting in actin redistribution and actomyosin contractility within minutes (Langevin et al., 2006) ultimately causing an increase in the fascial thickening. This process of thickening and densification of the fascia may explain the reduction of sliding potential between involved fascial layers and adjacent structures, as observed in patients with non-specific neck and low back pain (Tozzi et al., 2011; Langevin et al., 2011). Chronic conditions may ultimately result in fibrosis and tissue adhesions (Wynn, 2008). The latter has been shown to potentially initiate pain in distant structures, such as myofascial pain in adjacent tissues (Lewit & Olsanska, 2004). Also due to fascial ‘tensegrative’ behaviour (Ingber, 2008), any fascial dysfunction may easily cause body-wide repercussions from a gross macroscopic anatomy to a molecular level, potentially creating stress on any structure enveloped by fascia, hence requiring progressive body adaptation at a local and global level (Levin & Martin, 2012).

In 2014, Stecco et al., conducted a medium quality (PEDro: 5/10; CEBM: 2b) randomised controlled trial to understand the possible role of the deep fasciae in chronic neck pain (CNP) and the utility of the ultrasonography in the diagnosis of myofascial neck pain by comparing twenty five healthy subjects and twenty eight CNP patients. The fascial thickness of the Sternal ending of the Sternocleidomastoid and medial scalene muscles were analysed by ultrasonography along with other outcome measures. The study established significant differences between healthy subjects and patients with CNP in the thickness of the sternocleidomastoid and scalene fascia and the effect of facial manipulations on it at the end of the treatment and follow-up. The study ends by commenting that the loose connective tissue inside the fascia may play a significant role in the pathogenesis of CNP. The variation of thickness of the fascia correlated with the increase in quantity of the loose connective



tissue but not with dense connective tissue. Even though the study was in an RCT format, the methodological flaws and small sample size makes the generalisability under shadow. It is still unknown how the finding of the ‘increased fascial thickness’ could be used to explain the role of ‘loose connective tissue in the pathogenesis of CNP’ when the reliability of ultrasound itself is in question for fascial analysis. It should be appreciated that the fascia based experiments are advancing from the cadaver based anatomical observations to RCTs with real time observations.

### **1.3.1. c. Fascial Contractility**

It has been proposed that fascia may contract in a smooth muscle-like manner (Schleip et al., 2005), independently of skeletal muscle activity. This is possibly related to the presence of smooth muscle cells found in fascial tissue (Staubesand et al., 1997) and the capacity of myofibroblasts to contract via intracellular alpha smooth-muscle actin ( $\alpha$ -SMA) (Hinz & Gabbiani, 2003). This hypothesis was supported by in-vitro studies demonstrating an autonomous contraction of human lumbar fascia and a pharmacological induction of temporary contraction in porcine and rat fascial tissue when stimulated with various pharmacological agents i.e., mepyramine, angiotensine and glyceryltrinitrate (Masood & Naylor, 1994; Klingler et al., 2014). “An estimation of tension created by contraction of myofibroblasts when extrapolated to a large fascial sheet (i.e., thoracolumbar fascia) may produce tension within the musculoskeletal system between 30–40N” (Schleip et al., 2005). The significance of this contractile property remains hypothetical and reproduction of these contractile forces in-vivo in response to efferent neural stimulus is yet to be done (Kumka & Bonar, 2012; Wilke et al., 2017b).

Although, most myofibroblasts derive from regular fibroblasts modified under mechanical tensions and the influence of specific cytokines (Desmoulière et al., 2005), they can also originate from other tissues that include epithelial, endothelial and bone marrow-

derived cells (Hinz et al., 2007). Regardless of their origin, myofibroblasts are able to produce long lasting isometric contractions (Hinz & Gabbiani, 2003), transmitted to the matrix through focal adhesions and connected stress fibres. It has been suggested that the force generated by fascial contraction may extend to intramuscular connective tissues in order to adapt muscle stiffness to changes in tensional demands (Schleip et al., 2006). In turn, this is likely to influence overall resting muscle tone and musculoskeletal dynamics (Schleip et al., 2005) through both a local redistribution of mechanical force and a segmental neurological influence on somatic motor neurons.

Dysfunction of this apparatus may also lead to altered myofascial tonus, diminished neuromuscular coordination, musculoskeletal pathologies and pain syndromes (Klingler et al., 2014). Furthermore, dysregulated myofibroblastic activity may result in fibrosis formation and the development of chronic systemic diseases (Hinz et al., 2012).

The whole series of these events dysregulated myofascial contraction, altered myofascial tonus and force transmission, impaired neuromuscular coordination and fibrosis formation may lead to an abnormal fascial contractility and texture that underlies restriction of motion, functional and positional asymmetry, as found in somatic dysfunction (Tozzi, 2015b).

#### **1.3.1. d. Fascial Viscoelasticity**

Fascia exhibits the potential for both elastic and plastic deformation in a non-linear fashion, depending on the amount, duration and speed of the load (Kirilova, 2012). This viscoelastic property relies on the interdependence between the architecture and composition of connective tissue and water content (Guilak, 2000). It has been demonstrated that fibrils and the interfibrillar matrix may act as coupled viscoelastic systems, with a qualitatively different response to mechanical deformation, depending on the cross-links in between collagen molecular packing (Tozzi, 2015a).

At the same time, when tension changes in connective tissue, an immediate reorganization of the fibroblasts cytoskeleton occurs, with a consequent change in tissue stiffness and viscosity (Langevin et al., 2006), through changes in cell signalling, gene expression, matrix adhesions and consequent modification in connective tissue tension and biochemistry (Tozzi,2015b).

Human resting myofascial tone (HRMT) (Masi & Hannon, 2008); is determined by molecular interactions of the actomyosin filaments in myofibroblast cells and miosarcomeric units. This may offer a substantial contribution to the maintenance of postural stability with minimal energy expenditure, differently from neuromotor activation which requires higher levels of tone to provide the same stabilization. This is consistent with recent findings in pathological conditions. Persistent static load lead to viscoelastic creep of connective tissue, resulting in a transient alteration of neuromuscular activity (muscle spasm and hyperexcitability), with an intensity directly related to the load magnitude (Sbriccoli et al., 2004).

Similarly, prolonged repetitive cycling loading may alter viscoelastic properties of connective tissue by causing micro-damage of collagen fibres, necessitating increased muscular activation to maintain joint stability. This was a finding from a review of in-vivo feline studies in this area (Solomonow, 2012). Similar findings were observed in-vivo (Fung et al., 2009; Schleip et al., 2012c) and in controlled human laboratory studies (Sbriccoli et al., 2005; Arampatzis et al., 2010; Olson, 2011). The ‘construal’ difficulty was the main problem with the ‘Solomnov’ review as the study utilized a complex hypothesis and methodology that is triggering an interpretation or conclusion bias in the reader. Changes in normal levels of HRMT would affect the tension on surrounding fascial structures and have an influence on joint mobility, movement control, posture stability related to different musculoskeletal conditions and dysfunctions (Masi et al., 2010). The combination of these events may also be

associated with a change in the colloidal consistency of the ground substance to a more solid state and lead to altered myofascial activation, increased risk of tissue damage/injury, and finally account for the tissue texture change, restriction of motion and asymmetry found in somatic dysfunction.

### **1.3.1. e. Fascial Fluid Content and Dynamics**

Fascia also plays an important role in fluid balance and physiology. Water content is dependent on changes in interstitial fluid pressure resulting from a dynamic interaction between the osmotic pull exerted by negatively charged, normally under-hydrated Glycosaminoglycans that are abundant in fascia, and the mechanical stiffness and tension of collagen fibres that resist water extrusion and thus tissue swelling (Tozzi,2015a). It appears that any decrease in collagen tension leads to a reduction in interstitial hydrostatic pressure and causes fluids to be taken up by the constituents of the ECM. The role of fibroblasts is also crucial in determining collagen tension through cell-matrix contacts, acting as modulators of fluid dynamics by adjusting their size and matrix tension in response to changes in osmotic pressure (Langevin et al., 2013). In turn, hydrostatic pressure has been shown to act as a mechanical stimulus inducing cell-matrix processes of ‘mechanotransduction’ that directs cell behaviour in a variety of tissues, including cell movement within the ECM (Polacheck et al., 2014), cytoskeletal polymerization and cellular tuning of sensitivity to fluid pressure and to accommodate variable levels of stress (Myers et al., 2009). In particular, intermittent cyclic hydrostatic pressure applied to bone-derived cells induces alterations in mRNA levels for a specific subset of genes involved in connective tissue remodelling and differentiation (Tasevski et al., 2005). However, during inflammation, changes in physical properties of the connective tissue, involving hyaluronic complexes, may influence transcapillary exchange resulting in an increase in the fluid flow (Reed et al., 2010). This is caused by an integrin-mediated lowering in interstitial fluid pressure following a release of cellular tension exerted on the collagen network that allows

glycosaminoglycans to expand and take up fluids. Therefore, an inverse influence exists among mechanical force, cell response and interstitial fluid dynamics. This was a finding obtained from the study on ‘edema and fluid dynamics in connective tissue remodeling’. This review was a gathering of observations from studies of the loose connective tissues in skin and carcinomas performed in-vitro with relevant extrapolations and comparisons to the heart.

A sustained static stretch applied to fascia may produce an extrusion of water in the tissue followed by a compensatory increase in matrix hydration (Schleip et al., 2012c), resembling a sponge-like effect that may be significant for fascial function. This study examined a potential cellular basis for strain hardening of fascial tissues: an increase in stiffness induced by stretch and subsequent rest. The study was conducted in ‘mice’ lumbodorsal fascia which was isometrically stretched for fifteen minutes followed by thirty minutes rest (n=16). An increase in stiffness was observed in the majority of samples, including the nonviable control samples. Investigations with porcine lumbar fascia explored hydration changes as an explanation (n=24). Subject to similar loading procedures, tissues showed decreases in fluid content immediately post-stretch and increases during rest phases. When allowed sufficient resting time, a super-compensation phenomenon was observed, characterised by matrix hydration higher than initial levels and increases in tissue stiffness. The authors have cautioned that, with an in-vitro result generalisation and clinical application cannot be recommended and merits further exploration.

Stecco et al. (2011a) have shown that in normal physiological conditions, a layer of lubricating ‘hyaluronan’ (HA) is found between the deep fascia and muscle as well as within the loose connective tissue, dividing different fibrous sublayers of the deep fascia. These HA layers promote normal fascial function and sliding motion. If compromised, as following injury or chronic inflammation, they may underlie various types of myofascial dysfunctions and pain by impairing tissue sliding potential and fluid dynamics, hence tissue chemistry and structure.

The layers of loose connective tissue within deep fasciae were studied with particular emphasis on the histochemical distribution of HA. Samples of deep fascia together with the underlying muscles were taken from neck, abdomen and thigh from three fresh non-embalmed cadavers. Samples were stained with hematoxylin–eosin, azan-mallory, alcian blue and a biotinylated HA-binding protein specific for HA. An ultrasound study was also performed on twenty two voluntary subjects to analyse the thickness of these deep fasciae and their sublayers. This study introduced the term “fasciocytes” to the cells that stained prominently with alcian blue stain. This study was the one which provide some evidence on the role of HA in fascial mobility and its role in myofascial pain. Recent in-vitro and in-vivo studies are supporting and confirming these findings (Wilke et al., 2017b; Manfredini et al., 2017; e Silva et al., 2017).

#### **1.3.1. f. Fascial pH and Factors Influencing its Levels**

Changes in pH, ionic content and temperature may represent key environmental and metabolic factors influencing fascial viscosity (Thomas & Klingler, 2012). For instance, an increase in body temperature, as occurs during physical exercise, may reduce fascial stiffness by reducing tissue viscosity (Chaitow et al., 2014; Propert, 2014; Pavan et al., 2014). Pavan et al (2014) has made an attempt to segregate evidences for the influence of temperature and pH in fascial properties. An in-vitro analysis by Tømmeraas et al. (2008) found that three-dimensional superstructure of HA chains progressively breaks down when the temperature is increased to greater than 40 °C improving the fascial sliding. This may explain the effects of many physical therapies that increase temperature (laser, ultrasound etc.) and with warming up in general. The increased temperature breaks down superstructures, with a consequent decrease in viscosity. Also, alterations of pH can change the viscosity of loose connective tissue. Gatej et al, (2005) conducted a series of laboratory studies to analyse the behaviour of HA solutions at different pH values. A slight degradation is observed in acidic conditions (pH = 1.6) and

basic medium (pH = 12.6) from molecular weight distribution analysis, but the 'rheological' behaviour is relatively not influenced much by the pH at the exclusion of two domains: around pH of 2.5, a gel-like behaviour is shown and is attributed to cooperative interchain interactions due to the reduction of the polymer net charge and may be the protonation of the acetamido groups; for pH greater than 12, the decrease of viscosity is mainly attributed to a reduction of the stiffness of the polymeric backbone in alkaline conditions due to the partial breakage of the H-bond network.

The biomechanical properties of loose connective tissue may be altered depending upon accumulated lactic acid content after intense exercise, with its attendant acidity (Pavan et al., 2014). It has been demonstrated that in the muscle compartment, pH can reach a value of 6.60 with an increase of approximately 20 % in HA viscosity, with a consequent sensation of momentary stiffness. This finding was based on three non-randomised small group studies (Juel et al., 2004; Juel et al., 1990; Neilsen et al., 2004). In future, robust and standardised studies can explore more on this.

Conversely, a more acidic ECM environment seems to exert a modulating action on the metabolism and protein synthesis of connective tissue cells, such as fibroblasts and chondrocytes (Ohshima and Urban, 1992). In conclusion, changes in breathing patterns and temperature, and presumably of physical activities (Shen et al., 2012) and nutrition (Arent et al., 2010) are able to modulate tissue pH levels through environmental and metabolic changes, and oscillations of these may strongly influence fascial function and dysfunction. Many fascial therapists believe that the fascia can alter its behaviour in relation to various chemical and environmental factors. But at this point, none of the findings are conclusive. Capitalising on the works done hitherto and the resultant findings, future studies can look more vigorously and systematically into this area.

### ***1.3.1. g. Somatic Neuro-fascial Interaction***

A review by Benjamin (2009) describes several studies that showed the presence of primary afferents and nerve fibres within fascia, supporting the concept of fascia as a ‘sensory organ’. In particular, the presence of mechanoreceptors in fascia suggests a role in dynamic proprioception, force transmission and motor control (Stecco et al., 2010). Research also shows that fascia, rather than muscle tissue, is involved in the delayed onset of muscle soreness following physical exercise, suggesting a role in pain generation in normal physiological conditions (Gibson et al., 2009).

However, under abnormal mechanical stimulation, a pathological change in fascial innervation may occur, resulting in dysfunctional ingrowth of nociceptive fibres (Sanchis-Alfonso & Rosello´-Sastre, 2000) that generates or maintains inflammation (Herbert and Holzer, 2002).

Irritation of primary afferent fibres in the fascia is capable of initiating the release of neuropeptides, eventually setting up a neurogenic inflammation, with peripheral (Deising et al., 2012) and central sensitization, and altering the texture of surrounding connective tissue via the interaction of fibroblast and immune cells (Mense, 2001). This process may trigger a cascade of either local or global responses: chronic pain and connective tissue remodelling (Langevin et al., 2011), altered mechanoreceptor feedback and muscle control (Panjabi, 2006), followed by further connective tissue alterations, neural adaptation, and eventually cortical reorganization. This process may expand to include influences on endocrine and autonomic pathways (Benarroch, 2006), as well as on sensory, cognitive and affective areas of the brain that may in turn respond to control pain (Peyron et al., 2000). Schabrun et al. (2013) has conducted a small group healthy individual based study on somatosensory-evoked potentials (SSEPs) and transcranial magnetic stimulation to investigate the temporal relationship between



altered excitability of the primary sensory cortex and corticomotor output during and after muscle pain induced by hypertonic saline infusion and reported that pain of muscular origin may alter the activity of related higher centres accounting for a reduction of sensory processing, followed by an altered motor output, together with a reorganization of the motor cortex associated with deficits in postural control (Tsao et al., 2011).

Both structural and functional changes of the brain were noticed in patients with myofascial pain. Literature reported significant changes in grey and white matter anatomy. High-resolution voxel-based morphometric structural brain and brainstem scans are available to support this. The first report of central nervous system (CNS) changes in myofascial pain was in 2010, by Younger et al, Significant change (both decrease and increase) was noted in the grey matter volume as compared to controls mainly in the ‘trigemino-thalamocortical pathway’ (trigeminal sensory nuclei, thalamus and primary sensory cortex) and a decrease in grey matter volume was noted in the ‘limbic system’ (posterior putamen, globus pallidus and anterior insula). In another similar study, a regional decrease was found in white matter volume in the medial prefrontal cortex (PFC) bilaterally (Gerstner et al., 2011). Furthermore, a decrease in grey matter volume occurred in the cingulate gyrus, insular cortex, frontal gyrus, and superior temporal gyrus bilaterally in the temporomandibular disorder patients. When myofascial trigger points were stimulated (Niddam et al., 2008), enhanced activity was found in somatosensory (SI, SII, inferior parietal, mid-insula) and limbic regions (anterior insula) and suppressed activity was found in the hippocampal area. In a positron emission tomographic (PET) study (Kupers et al., 2004), it was shown that induced jaw-muscle pain (a chronic pain model that mimics fascial pain) was associated with a significant increase in regional cerebral blood flow in the posterior insula, anterior cingulate, prefrontal cortices, right posterior parietal cortex, brainstem, cavernous sinus and cerebellum indicating them as potential areas involved in assimilating jaw pain.

### **1.3.1. h. Autonomic Neuro-fascial Interaction**

Fascial tension may be regulated via autonomic activity, independent of skeletal muscle tone. This may occur through the interaction of autonomic fibres and smooth muscle cells found in fascia that may consequently contract in a smooth-muscle like manner (Schleip et al., 2005). Therefore, because under mechanical tension and through a mechano-transduction process, fibroblasts release 'Transforming growth factor beta-1'(TGF-b1) that in turn promotes myofibroblast differentiation and contractility by increasing a-SMA (alpha-smooth-muscle actin) expression (Wipff et al., 2007), it has been suggested that sympathetic activation may induce myofibroblast contraction in fascial tissue via the release of TGF-b1, as well as other cytokines, hence modulating fascial stiffness (Schleip et al., 2012b). In addition, they may play a role in pain modulation by activating sensitized primary afferent fibres, either directly or indirectly, and thus contributing to the development of chronic myofascial pain syndromes (Stecco et al., 2014). Therefore, autonomic activity may be involved in the genesis or maintenance of pain and somatic dysfunction in the connective tissue (Tozzi, 2015b).

### **1.3.1. i. Piezoelectricity**

Piezoelectricity is a property associated with a variety of biological structures ranging from bones to proteins and nucleic acids (Fukada, 1982). It is based on an electromechanical coupling by which a mechanical force is converted into an electrical stimulus through a stress-induced polarization and vice versa. One of the main components of fascia is collagen. It has already been shown proteins including collagen can display semi-conductive, piezoelectric and photoconductive properties in vitro (Yang et al., 2015). Electronic currents can flow over much greater distances than ionically derived potentials. These electronic currents within connective tissue can be altered by external influences, and cause a physiologic response in neighbouring structures (Langevin, 2006). However, exploration of the change in bone structures in response to stress (Wolffs law) suggests that

fluid flow within tissue is more important than piezoelectric effects (Ahn & Grodzinsky, 2009). Collagen may exchange physical information from a macroscopic to a cell scale, either directly or via biochemical process (Stroe et al., 2013).

Although collagen generates different piezoelectric charges based on the type and intensity of the stress applied (Ahn & Grodzinsky, 2009), an intrinsic piezoelectric heterogeneity has been shown to exist within a collagen fibril, and is related to periodic variations in its gap and overlap regions. Each single collagen fibril has a unipolar axis polarization throughout its entire length, with a piezoelectric coefficient on the order of one pm/V (Minary-Jolandan & Yu, 2009). The problems of these finding were that both are analytical reviews and these observation were regarding the collagen of bone rather than fascia.

With regard to fascia, the piezoelectric properties of collagen fibrils were first imaged by Harnagea et al. (2010) with a ‘sub-twenty nm’ spatial resolution ‘piezoresponse force microscopy’ (PFM). A detailed analysis of the PFM signal in controlled tip-fibril geometry revealed shear piezoelectricity associated with piezoelectric deformation along the fibril axis, with the direction of the displacement being preserved along the whole fibre length, independently of the fibre conformation. The study has also shown that collagen fibrils in muscular fascia display an organization in domains, with groups of fibres with same polar orientations and others in the opposite one. The study has also shown that collagen fibrils in muscular fascia display an organization in domains, with groups of fibres with same polar orientations and others in the opposite one. This study was piloted in a mice tibialis anterior fascia harvested in situ.

Denning et al. (2017) have conducted a similar study on the piezoelectric properties of rat tail tendons. The tendons were sectioned at angles of 0, 59, and 90° relative to the plane orthogonal to the major axis, and were measured using PFM. The piezoelectric tensor at the length scale of an individual fibril was determined from angle-dependent in-plane and out-of-

plane piezoelectric measurements. The longitudinal piezoelectric coefficient for individual fibrils at the nanoscale was found to be roughly an order of magnitude greater than that reported for macroscopic measurements of the tendon and concluding that the low response to the macroscopic level may be due to presence of oppositely oriented fibrils.

It seems that the physicochemical properties of collagen critically depend on its hierarchical structure. Tropocollagen molecules, the basic units of collagen, have been shown to be arranged in a crystallographic super lattice with a quasi-hexagonal symmetry (Orgel et al., 2006), while collagen fibres display a D-periodic spacing within fibril bundles and at different levels of hierarchical complexity (Fang et al., 2012). The piezoelectric response seems to be directly proportional to the level of order by which molecules of collagen fibrils are assembled, including the D-periodicity (Denning et al., 2014).

These findings may help in understanding biological functions of fascia and the processes by which cells assemble collagen fibrils in response to specific directional mechanical forces. In fact, piezoelectric currents generated by mechanical strain on collagen fibres during wound formation have been proposed as driving forces in the first stages of tissue repair, acting in concert with TGF- $\beta$  to determine collagen fibres deposition and orientation (Farahani & Kloth, 2008). In conclusion, it is plausible that alterations of collagen architecture following injury, surgery or chronic inflammation, may lead to changes in piezoelectric responses of the area involved, with consequent repercussions on fascial function and structure (Tozzi, 2015b).

### **1.3.1. k. Water**

Sommer et al. (2008) suggest that interfacial water plays a key role in protein folding, cell to cell recognition and behaviour. Every collagen fibre in the body is embedded in layers of water molecules that, when associated with proteins, behave in a highly ordered and

patterned, or crystalline, manner (Pollack et al., 2006). It may also serve for bioenergy transport, mainly released by hydrolysis of adenosine triphosphate. In addition, the hydrophilic interactions of hydrogen bonds that stabilize this system may support non-linear fast transfer of protons through the molecular structure. It is plausible that fascial dysfunction may rise from dysfunctional self-reinforced circuits of proton-electron-hydrogen transfers following structural alteration of the collagen bound- water network, as may occur in injury, inflammation and scar tissue (Tozzi, 2015a).

### **1.3.1.1. Myofascial Force Transmission**

Functional myofascial sequences are directly involved in the organization of movement and muscular force transmission (Kwong & Findley, 2014; Myers, 2009; Stecco et al., 2010). Dense connective tissues and tendons are predominantly aligned type I collagen and are more specialized for force transmission (Huijing, 2009; Maas & Sandercock, 2010). Forces exerted by any one muscle are known to transmit longitudinally along the myotendinous junction to exert an action across a joint. However, these forces may also be transmitted epimuscularly between muscle fibres and fascial connective tissues (Huijing, 2009; Maas & Sandercock, 2010). In fact, up to 30 percent of muscle tension may be transmitted via extramuscular force transmission (Huijing et al., 2003). Myofascial connections between muscles are involved in the force transmission of one muscle to a neighboring one, and even to antagonistic muscles.

Additionally, force transmission from muscles to surrounding fascia may cause stretching and tension (Stecco et al., 2010). It is proposed that these fascial expansions allow reciprocal feedback between fascia and muscles. These physical connections also suggest that forces and states of contraction may be transmitted and perceived not only locally but also at farther distances (Kwong & Findley, 2014).

### **1.3.1. m. Mechanotransduction**

The mechanical force transmission that occurs at the macroscopic level may affect tissues at the cellular level. Fascia contains fibroblasts which are involved in the synthesis of the extracellular matrix. Fibroblasts have been well studied in the wound healing literature (Desmoulière et al., 2005). Fibroblasts can develop into myofibroblasts with stretching and certain biochemical signalling such as transforming growth factor beta-1 and extra domain A fibronectin. The myofibroblast expresses more alpha smooth muscle actin and has a phenotype with increased contractile force capacity (Kwong & Findley, 2014).

Morphological transformations of fibroblasts have been studied in three-dimensional in-vitro matrices. It was found that, at rest, fibroblasts are in a dendritic state (Chiquet et al., 2009). When a stretching force was applied to the matrix environment, fibroblasts changed into an expanded lamellar morphologic state. Mechanical stimuli can modulate cell signalling, gene expression, matrix adhesion and connective tissue tension (Chiquet et al., 2009; Langevin et al., 2010). Repetitive mechanical straining of fibroblasts in a two-dimensional model induces changes in cellular proliferation as well as secretion of inflammatory mediators (Dodd et al., 2006).

Because of mechanotransduction, cellular changes of fibroblasts within fascia may occur in response to these external forces. Connective tissue remodeling may occur, in turn affecting function. Thus, the role of fibroblasts in cellular events of tissue remodeling during day-to-day activities, exercise, injuries, and therapies needs to be further explored (Kwong & Findley, 2014).

### **1.3.1. n. Sliding**

Interfaces between fascial layers and other structures can allow them to slide upon one another. The term “microvacuolar system” has been used to describe the types of connections between fascial structures visualized using fibre optic cameras under the dermatological layers

(Guimberteau et al., 2010) that may allow sliding. But it is not a specific structure in itself. These connections were also examined using electron microscopy and multiple polyhedral microvacuoles of different sizes and shapes were seen. This microvacuolar system is thought to be composed primarily of proteoglycans (Guimberteau et al., 2010). Proteoglycans, specifically glycosaminoglycans, have a high density of negative charges and can thereby draw in water molecules, forming gels at very low concentrations (Chaudhry et al., 2014). As such, it is proposed that this microvacuolar system contains water and has viscoelastic properties, behaving like a gel. It likely provides lubrication and absorbs shear stresses, which results in nearly frictionless musculotendinous movement. This described sliding system may actually be equivalent to the loose connective tissue of the extracellular matrix (Kwong & Findley, 2014).

A prominent layer of loose connective tissue resides between deep fascia and the epimysium of the underlying skeletal muscle (Stecco et al., 2011a). There are also similar and less prominent layers within the deep fascia itself. These layers were found to be rich in hyaluronic acid (Stecco et al., 2011a) which is one of several groups of glycosaminoglycans (Alberts et al., 2002). The density of the extracellular matrix may depend on the concentration of this hyaluronic acid and factors such as temperature or possibly other physical parameters. Based on their observations, Stecco et al. (2011a) theorized that this substance, along with water, might create the smooth gliding between the surfaces of fascia and muscle, between different fascia sublayers and also between different motor units. Any alteration of the hyaluronic acid can theoretically change the properties of the extracellular matrix, affecting sliding. This may lead to restrictions in sliding and modification of the receptors within fascia and is also theorized as a potential cause of myofascial pain (Stecco et al., 2013)

### **1.3.1. o. Innervation**

Studies have shown that intense local and referred pain occurs with injection of hypertonic saline into the tendons and fascia (Gibson et al., 2009; Schilder et al., 2014). Injections into tendon and tendon-bone junction sites were found to be more sensitive than injections into the muscle belly (Gibson et al., 2009). Sensitivity to pain was not found to be a strictly volume-driven process because ultrasound-guided injections of isotonic saline into fascia resulted in less pain than hypertonic saline injections even though both fluids distended the fascia (Schilder et al., 2014). The innervation profile of fascia may partially explain why these injections result in pain.

For example, thoracolumbar fascia plays a role in low back pain (Ranger et al., 2016). Although Bednar et al. found that thoracolumbar fascia was deficiently innervated (Bednar et al., 1995), Yahia et al. (1992) reported free nerve endings and mechanoreceptors. Tesarz et al. (2011) found that the thoracolumbar fascia and the overlying subcutaneous tissue are densely innervated, including nociceptive and sympathetic fibres. Nerve fibres were present in high densities in the outer and subcutaneous tissue layers, but not so in the middle layer. The presence of sensory fibres in the superficial layers may contribute to painful sensations experienced during manual therapies for back pain. Ranger et al. (2016) concluded that a shorter lumbar paraspinal fascia is associated with high intensity low back pain and/or disability among community-based adults. Schilder et al. (2016) have found that electrical high-frequency stimulation of the human thoracolumbar fascia evokes long-term potentiation-like pain amplification and concluded that spinal input from the fascia can induce long-term changes in pain sensitivity for at least 60 minutes making it a candidate potentially contributing to nonspecific low back pain

However, fascial innervation may not only be restricted to nociceptive fibres. Immunohistochemical staining of ankle retinacula revealed small nerve fibres and corpuscles



within ankle retinacula (Stecco et al., 2010). Interestingly, the intrafascial nerves were often oriented perpendicular to the collagen fibres which suggests that they could be stimulated by stretching of the collagen fibres. Besides free nerve endings, various fascial expansions have been shown to have encapsulated receptors such as Ruffini and Pacini corpuscles, suggesting a static and dynamic proprioceptive function (Stecco et al., 2010). Furthermore, muscle spindles tend to be located in areas of the muscle where the architecture suggests lateral myofascial force transmission, indicating there is no clear division between “muscle” and “ligamentous or fascial” nerve endings (van der Wal, 2009).

If the periarticular regular dense connective tissue is thought of in series with the periarticular muscle, collagen fibres within fascial tissue around joints may be stretched with movement. Any contraction of the muscles results in a simultaneous stretch of the fascial tissue. If these tissues contain free nerve endings and mechanoreceptors, then any dysfunction of fascial structures may potentially play a large role in pain or influence proprioception (Kwong& Findley, 2014).

### **1.3.1. p. Fibrosis and Densification**

The terms “fibrosis” and “densification” are often used to indicate alterations in fascial structures (Pavan et al., 2014, 2016). Fibrosis is similar to the process of scarring, with the deposition of excessive amounts of fibrous connective tissue, reflective of a reparative or reactive process. It can obliterate architecture and function of the involved tissue. Densification indicates an increase in the density of fascia. This is able to modify the mechanical proprieties of fascia, without altering its general structure. Dupuytren’s disease and eosinophil fasciitis could be considered typical examples of fascial fibrosis, while chronic and nonspecific neck pain seems to be associated with fascial densification (Stecco et al., 2014). In reality, in the majority of cases, it is not clear whether it is fascial densification or fascial fibrosis that is involved. This lack of certainty not only causes confusion in terminology, but also implies that

very different treatment modalities can be applied to fascia in an attempt to relieve pain (Stecco et al., 2014; Pavan et al., 2016).

### **1.3.1. q. Hysteresis**

In general, hysteresis can be defined as the amount of energy lost during a loading–unloading cycle in a tissue. In fact, in relation to tendon structure, the reduction of the hysteresis of deep fascia with the increase of loading rate improves the capacity of elastic energy storing and recoiling (Martin et al., 2015). The main components of the loose connective tissue are water, ions and glycosaminoglycans, with a prevalence of hyaluronic acid (HA) which allows normal gliding of joint and connective tissue. HA is secreted by specific cells inside the fascia called ‘fasciocytes’ (Stecco et al., 2011a).

Possible alterations of the deep fasciae could be at least of two different kinds: (i) damage of the loose component that affects the sliding system between different layers, and (ii) damage of the fibrous component that affects the capacity of loading transmission (Pavan et al., 2014).

The complex structure of deep fasciae is associated with different kinds of pathological changes. If there is only an alteration of the loose connective tissue, the term ‘fascial densification’ is probably preferred. If there is alteration of collagen fibrous bundles, ‘fascial fibrosis’ is the term of choice. In reality, the two alterations are not incompatible (Chaitow, 2014; Pavan et al., 2016).

Pavan et al. (2014) have put forward two possibilities. (i). Diet, exercises and overuse syndromes may cause an alteration of the loose connective tissue inside the deep fascia, causing fascial densification. (ii). Trauma, surgery and diabetes can alter the fibrous layers of the deep fasciae, causing a fascial fibrosis. This alteration is difficult to modify because only a local inflammatory process can destroy the pathological collagen fibres and permit deposition of new collagen fibres. Mechanical tensile stimulation can significantly enhance cell proliferation

in the fascia. The mechanism underlying the therapeutic effect of complementary therapies may involve the reconstruction of the loose connective tissue and enhancement of the cell proliferative activity under tensile load (Pavan et al., 2014). These are hypotheses (only) which need future confirmation.

### **1.3.1. r. Tensegrity**

The contraction of myofibres mechanically influences the endomysium, perimysium and epimysium and leads to shortening of the entire muscle because of their tensional continuity with each other and the tendinous tissues at each end. This balance between tension and compression acting within and between different tissues has been considered in relation to ‘tensegrity’ (tension-integrity) (Scarr, 2011). It is a structural mechanism that potentially integrates anatomy from the molecular level to the entire body and is popularly recognized for its distinct compression elements that appear to float within a tensioned network. It is an attractive proposition in living organisms because such structures maintain their energy-efficient configuration even during changes in shape. It has been described at higher levels in the extracellular/fascial matrix and musculoskeletal system. The helix and tensegrity are described in a variety of anatomical structures, suggesting their importance to structural biology and manual therapy (Scarr, 2014).

## **1.3.2. Disorders of the Superficial Fascia**

### **1.3.2. a. Fascia and Lymphedema**

In a narrative review, Stecco et al. (2016) mentioned that there exists a strong relationship between lymph vessels and superficial fascia and postulated that any alteration in the superficial fascia can cause lymphedema or a patient with lymphedema can have an alteration of the superficial fascia. They suggest that any treatment that involves superficial fascia should improve the symptoms related to lymphedema. This narrative review was

performed by the principle author on articles taken from PubMed database using keywords that contain “fascia.” The research included articles published between 2000 and 2015 with a total of seventy nine articles involving various noninvasive treatments with a level of evidence of 3b or above as per the CEBM Scale. Since this study does not fit in a systematic review category, the conclusions and findings need to be read with caution.

Tassenoy et al. (2009) published a case study on irreversible post-mastectomy lymphedema by comparing histological findings with Magnetic Resonance and Ultrasonographic imaging. The study found that the adipose tissue, inferior to the superficial fascia, has a honeycomb appearance as established by magnetic resonance imaging (MRI). This corresponds to fluid associated with the fibrosis. In particular, the skin septa or fibrous retinacula cutis increase their thickness, the area and perimeter of fat cells is significantly increased ( $P < .05$ ) and fluid is associated with or close to the muscle fascia.

Marotel et al (1998) conducted a retrospective analysis of the computer tomography (CT) data from eleven patients with isolated unilateral lower limb lymphedema (clinical criteria confirmed by isotope lymphography). This study has found an increase in the frequency of skin thickening, increase in the subcutaneous tissues area, muscular fascia thickening, fat infiltration and oedema relate to lymph stasis. The reliability of CT images in detecting such micro details of the soft tissue made this study finding in question.

Hauck and Castenholz (1992) through their microscopic analysis demonstrated the existence of a “low-resistance pathway” along connective tissue fibres for the trans-interstitial fluid movement, from the capillaries to the initial lymphatics. One part of this pre-lymphatic system is represented by submicroscopical spaces along the connective tissue fibres between ground substance (high resistance pathway) and fibre surface. The other part is represented by a network of pre-lymphatic tissue channels which are open connected with the initial lymphatic system.

Based on this finding, Stecco et al. (2016) concluded that the disposition of the collagen and elastic fibres inside the superficial fascia could guide lymphatic flux in the correct direction and any alteration in the superficial fascia can compromise the lymphatic drainage. Even though these findings are based on low to medium quality laboratory and imaging studies, the findings can be used to explain the positive results reported in a few randomised controlled studies on the effectiveness of myofascial release in post mastectomy patients (Castro-Sánchez et al., 2011a,b; De Groef et al.,2017). It is worth mentioning that the ultrasound measurement of dermal thickness is a reliable option to assess lymphedema following mastectomy as per the study by Dylke et al. (2017) and can help in facilitating, in future, high-quality studies in this field.

### **1.3.3. Disorders of the Deep Fascia**

#### **1.3.3. a. Myofascial Pain**

Deising et al. (2012) injected nerve growth factor into the fascia of the erector spinae muscles at the lumbar level and observed a long-lasting sensitization to mechanical pressure and to chemical stimulation. This suggests that sensitization of fascial nociceptors to mechanical and chemical stimuli may contribute to the pathophysiology of chronic musculoskeletal pain.

Schilder et al. (2014) have also demonstrated that injections of hypertonic saline into the thoracolumbar fascia result in a significantly protracted time of pain intensity, compared to injections into the subcutis or into muscle. Stecco et al. (2014) documented a correlation between a decrease in range of motion and an increase in neck deep fasciae thickness. In particular, a value of 0.15 mm of the sternocleidomastoid fascia is proposed as a cut-off value that allows the clinician to make a diagnosis of myofascial disease in subjects with chronic neck pain.

### **1.3.3. b Alterations in Proprioception**

The first to suggest a possible role of the deep fasciae in proprioception was Viladot et al. (1984). This was a pure anatomical study done on 118 ‘tali and calcanei’ obtained from cadavers and collections. The authors affirmed that as the ankle retinacula (which represent specialization of the deep fascia) are thin and flexible, they have a modest effect on the mechanical stability of the joint, whereas they have a far more important role in proprioception. Pisani (1990), in a similar study, concluded that the histological features of the retinacula are more suggestive of a perceptive function, whereas the tendons and ligaments are structured for a mechanical role. The retinacula are the most highly innervated fascial tissues. Sanchis-Alfonso & Rosello-Sastre (2000) demonstrated an increase in free nerve endings and nerve in-growth in the shortened compressed lateral retinaculum in patients with patellofemoral malalignment and anterior knee pain. Samples of lateral knee retinacula were excised at the time of proximal realignment or isolated lateral retinacular release.

The first in-depth focus on the role of fascia in proprioceptive function came from Stecco et al. (2004, 2006). They, with the cadaveric analysis details, suggested that “the presence of many free and encapsulated nerve terminations indicates that the deep muscular fascia probably plays a proprioceptive role” (Stecco et al., 2006, p 5). Stecco et al., in 2007(b), published yet another cadaveric analysis study based on specimens taken from the deep fascia from 20 human upper limbs. The main aim was to find out type of nerve fibres and endings in the deep muscular fascia. This study demonstrated an abundant innervation of the fascia consisting in both free nerve endings and encapsulated receptors, in particular, Ruffini and Pacini corpuscles. The study verified the differences in innervation as the flexor retinaculum was found more innervated than ‘lacertus fibrosus’ and the pectoralis major expansion. The authors suggest that these findings point out the role of the retinaculum in peripheral motor coordination and proprioception whereas the tendinous expansions onto the fascia with a

mechanical role in the transmission of tension. In the conclusion session, the authors were attempting to expand the fascial role in dynamic proprioception along with the static one. The team quotes the laboratory based works of Grigg & Greenspan (1977), Clark et al. (1975 a,b) and Rossi & Grigg (1982) to explain how joint receptors are activated only at maximum flexion and extension, placing doubts on the exclusive role of articular receptors in kinaesthesia. This fact further implicates intramuscular and fascial receptors as indicators of the intermediate grades of movement. This study puts forward an advanced hypothesis that all the fascia and/or the myofascial unit has a role in proprioception, particularly in dynamic proprioception (Stecco et al., 2004). The drawback of this study was that the hypothesis was too advanced beyond the scope of a cadaveric study so that the role of fascia in ‘dynamic proprioception’ should be interpreted with caution.

In 2010, Stecco et al conducted a study by dissection, histological and immunohistochemical analysis of twenty seven cadaveric legs along with an in-vivo radiological study by MRI on seven healthy volunteers, seventeen patients with outcomes of ankle sprain and three amputated legs. The aim was to anatomically ascertain the role of the retinacula in proprioception and their possible damage in patients with ankle sprain. The study specified that the retinacula are not static structures for joint stabilisation but a specialisation of the fascia for local spatial proprioception of the movements of foot and ankle. Their anatomical variations and accessory bundles may be viewed as morphological evidence of the integrative role of the fascial system in peripheral control of articular motility. Once again it is to be noted that, taking in to account of the complicated structure of the study, its assumption should be taken as preliminary and warrants more structured high quality biomechanical based human studies. Stecco et al. (2011b) re-demonstrated with MRI and static posturography in twenty five patients with ankle sprain that ankle sprain leads to damage to ankle retinacula (adherences and formation of new fibrous bundles into the deep fasciae of the foot and

interruption of the retinacula). Damage to the retinacula and their embedded proprioceptors result in inaccurate proprioceptive afferentation, leading to functional ankle instability (Stecco et al., 2011b). This may result in poorly coordinated joint movement and eventual inflammation and activation of nociceptors. The study concluded that a treatment focused on restoring normal fascial tension may improve the outcome of ankle sprain. This study falls in low methodological quality due to the methodological flaws and non-randomised design but the results can be used to create hypothesis for future scientifically robust studies (Stecco et al., 2011b).

#### **1.3.4. Epimysial Fascia and Peripheral Motor Coordination**

The epimysial fascia plays a key role in proprioception and peripheral motor coordination due to their close relationship with muscle spindles. Due to these connections, it is evident that tension developed inside the deep fascia is also able to lengthen the muscle spindles connected with it, activating them by passive stretch. If epimysial fascia is overstretched, it is possible that the muscle spindles connected to this portion of the fascia could become chronically stretched and over activated. This implies that the associated muscular fibres will be constantly stimulated to contract (Stecco et al., 2016). This could explain the increased amount of acetylcholine found in myofascial pain and, in particular, in trigger points (McPartland, 2004). This passive stretch situation could be responsible for muscular imbalances and recurrent cramps and could result in incorrect movement of joints. This may represent a typical case in which there is limitation of joint range of motion and associated joint pain. Palpation of the proximal muscle belly will often reveal an area of a painful localization of dense tissue. If epimysial fascia is too rigid, the muscle spindle may not be activated, some parts of a muscle will not function normally during movement, causing an unbalanced movement of the joint, with resulting uncoordinated movement and eventual joint



pain. This emphasizes the fact that normal muscular function is dependent on normal, well-hydrated and functioning fascia (Stecco et al., 2016).

Jafri (2014) presented a comprehensive descriptive overview of the underlying hypothesis, theories and evidence for the mechanisms of myofascial pain and trigger points (TrPs). According to this review, the mechanisms that induce the onset and maintenance of TrPs are unknown. Jafri postulates a new mechanistic hypothesis for the initiation and maintenance of TrPs. This hypothesis identifies an increased microtubule density, eventually leading to an increase in reactive oxygen species (ROS) levels and calcium in the TrP region.

#### **1.4. Defining Myofascial Release**

Myofascial release (MFR) is a form of manual medicine which involves the application of a low load and long duration stretch to the myofascial complex, intended to restore optimal length, decrease pain and improve function (Barnes, 1990). It has been hypothesized that fascial restrictions in one part of the body cause undue tension in other parts of the body due to fascial continuity. This may result in stress on any structures that are enveloped, divided, or supported by fascia (Schleip, 2003).

Myofascial practitioners believe that by restoring the length and health of restricted connective tissue, pressure can be relieved on pain sensitive structures such as nerves and blood vessels. MFR generally involves slow, sustained pressure (120-300 s) applied to restricted fascial layers either directly or indirectly. Three main manual approaches that are directed towards the fascia are (i) direct approach - the affected tissue is brought against the restrictive barrier, described as a “functional limit that abnormally diminishes the normal physiologic range” (E.C.O.P., 2011a). This is maintained until tensions modify. (ii) indirect approach - tissues are brought away from the restrictive barrier while a position of ease (a balanced tension in all planes and directions) is found and maintained up to a release. (iii) combined approach -

both the point of ease and the restrictive barrier are consecutively engaged in an interactive fashion (Ward, 2003). Direct technique MFR is thought to work directly on restricted fascia; practitioners use knuckles or elbow or other tools to slowly sink into the fascia, and the pressure applied is a few kilograms of force to contact the restricted fascia, apply tension, or stretch the fascia. Indirect MFR involves application of gentle stretch- the pressure applied is a few grams of force and the hands tend to follow the direction of fascial restriction, hold the stretch and allow the fascia to ‘unwind’ itself. The rationale for these techniques can be traced to various studies that investigated plastic, viscoelastic and piezoelectric properties of connective tissue (Schleip, 2003; Greenman, 2003; Pischinger, 1991).

Treatment of fascia has shown to be effective for a wide variety of conditions, from local musculoskeletal causes, such as acute joint injury (Eisenhart et al., 2003) to general mood disorders such as depression (Plotkin et al., 2001) thought to be because of the common therapeutic influence and stimulation of the myofascial complex (Simmonds et al., 2012).

William Neidner, in the early '20s, was the first to describe fascial torsion patterns in healthy and unhealthy individuals and one of the first to introduce to the osteopathic field a specific fascial approach, defined as fascial twist (Centers et al., 2003). By observing and palpating the entire fascial organization of the body, he noticed that people in good health tend to show clockwise fascial torsional patterns from head to feet (Frymann, 2004). He then proposed that various types of direct manipulative techniques could globally release such myofascial torques, through the use of the limbs as long levers for the untwisting manoeuvre (DeStefano, 2011). Still's concept of fascia continued to be developed by the early osteopaths and created the basis for much of our clinical understanding of this tissue which is increasingly recognized as the unifying structural element of the body and key to understanding the reciprocal interrelation between structure and function and the body's innate ability to self-

regulate (Snyder, 1956). These principles then led to the development of manual approaches that went beyond the structural model of treating articular joints.

In the 1980s, Ward's biomechanical model emphasized the muscular-fascial relationship and their interdependent neural influences and led to myofascial release and integrated neuromusculoskeletal release techniques (Ward, 2003) while Chila's (2003) fascial continuum model of the 'big bandage' introduced fascial release and fascial ligamentous release techniques based on the integrity of the fascial continuum (Chila, 2003). The same period also saw a gradual shift towards other methods based on oscillatory motion as an intrinsic tissue property with Sutherland's model of cranial and balanced ligamentous tension treatment (Sutherland, 1998) and Frymann's approach to fascia as the primary tissue to unwind any traumatic force imposed in the organism. Fulford's vibratory model (Fulford and Stone, 1997) and Becker's fluid approach then developed these further: "allow the fluid to resume its normal tidal mechanism 'bend to the oar' through the fascia and 'ride the tide to the shore' by way of the fluid" (Becker, 2000). In addition, the respiratory-circulatory model of Zink (1977) implied the assessment of compensated and uncompensated fascial patterns together with the opening of fascial pathways to restore and maintain homeostatic balance (Zink and Lawson, 1979). The bioenergetic model of O'Connell considered the bioresponsive electric potentials of fascia as changing holographically, as a result of the intention, attention and activation processes that occur during assessment and treatment (O'Connell, 2000).

The effects of manual fascial interventions can be local (as tissue texture changes), segmental (as via neurological response) and global (as through hormonal effects) in extent, and may occur at different intervals—ranging from minutes to weeks—after a given input, with many interacting mechanisms influencing tissue properties and behaviours, including placebo. Some of these factors are strongly supported by the available evidence whereas others need further investigation (Tozzi, 2015b).

## **1.4.1. Fascia-related Mechanisms Involved in the Treatment of Somatic Dysfunction**

### **1.4.1. a. Structural Changes**

In 2009, Langevin et al. performed an ultrasound-based comparison of perimuscular connective tissue structural variation in the lumbar region in a group of 60 human subjects with chronic or recurrent low back pain (LBP) compared to a group of 47 subjects without LBP. The study was set with good internal validity but with questionable external validity. The study was neither designed in a randomised format nor with blinding or concealing. The non-interventional format can be a justifiable answer to such arguments but no details of the possible biases were explained in the study. The authors were pointing out that this finding cannot be generalised to the patients who have had low back pain for less than twelve months and recommends future longitudinal studies. Nevertheless, this study concluded that LBP group had around 25% greater perimuscular thickness and echogenicity compared with the no-LBP group. In a similar quality study with one hundred and twenty one human subjects with and without LBP, Langevin et al. (2011) proved that thoracolumbar fascia (TLF) shear strain was almost 20% lower in human subjects with chronic low back pain. The authors were attributing this to the abnormal trunk movement patterns and/or intrinsic connective tissue pathology. There appears to be some sex-related differences in thoracolumbar fascia shear strain that may also play a role in altered connective tissue function. In a porcine model study, Bishop et al. (2016) has performed an ultrasound based evaluation of the combined effects of TLF injury and movement restriction and found that the combination of injury plus movement restriction had additive effects on reducing fascia mobility with a 52% reduction in shear strain compared to controls and a 28% reduction compared to movement restriction alone. These results suggest that a back injury involving fascia, even when healed, can affect the relative mobility of fascia layers away from the injured area, especially when movement is also

restricted. Robust quality human subject research in this area may enlighten the role of fascia and fascial release in the low back pain.

In a conference proceeding, Blanquet et al. (2010) concluded that ultrasound evaluation could be used to measure and explain the changes in the TLF post MFR. The study was carried out to find out the effectiveness of fascial release in TLF on ten human subjects with chronic LBP with readings taken before, immediately after and 24 hours after the treatment. Release of the thoracolumbar fascia in patients with chronic LBP has shown an increase in thickness of fascial layers that remained for at least 24 hours. The authors implied that the findings of the study can be used to explain the fascial changes in response to treatments and ultrasound evaluation can be a better tool to reflect these changes. The structure of the conference abstract without details like randomization and blinding along with a low sample size restricts the study's quality and generalisability. A study by Pohl (2010) has shown that ultrasound measurements applied immediately before and after manual intervention resulted significant differences in collagen fibre density and orientation in the structure of the matrix in the dermis, reflecting palpable differences in tension and regularity. Thirty patients were measured with high frequency ultrasound immediately before and after the first treatment in the area of pain or movement restriction. The result of the study is not foolproof due to the limitations associated with its validity and issues related to sampling. We need to conduct methodologically strong studies to ascertain such findings. All these findings are consistent with the assumption of re-organization and remodelling of collagen fibres, as suggested by Martin, (2009) explained as due to the breakdown of abnormal collagen cross-links and an increase in the matrix hydration which needs to be confirmed experimentally.

Wong et al. (2017) has conducted a cross sectional study with ten healthy participants to evaluate the mechanical deformation of TLF with myofascial release. An ultrasound evaluation was conducted before and after a press-down to maximal voluntary contraction

(MVC) in the prone position with three one minute procedure resembling to indirect Myofascial release techniques (IDTMFR). The study found that after MFR, the stiffness of the TLF decreased in healthy men. This was the first study to quantify fascial properties and deformation of the TLF and the effects of MFR on the TLF. The authors mentioned that they have conducted a pilot study with five participants in order to explore the reliability of each parameters and claims moderate to good reliability. A number of limitations were mentioned in the study including inability in the exclusion of isometric contraction and the measures taken for it, lack of control group, ultrasound image variability due to individual differences questioning test retest reliability and low sample size affecting generalisability. It cannot be possible to say that the TLF of healthy persons and one with chronic LBP behaves in a same way. It is doubtful whether one minute of IDTMFR is an ideal dosage to find a result as the minimum dosage used in this method is about three minutes. The data and limitations from this study can be used to design future methodologically robust randomised controlled studies on MFR. Future studies can analyse the effect of various forms of MFR with varying duration and frequency to ascertain and clarify these findings.

#### **1.4.1. b. Cell-based Mechanisms**

Various forms of manual loading, whether sustained or cyclical, that differ in direction, speed, magnitude and frequency appear to exert a strong impact on cell behaviour, gene expression and tissue remodelling through growth factors and enzyme activation (Tozzi,2015a).

Fibroblasts in-vitro and in-vivo have shown an almost immediate response to traction, pressure and shear forces, followed by a series of changes in chemical signalling pathways and gene activation, ATP release, actin polymerization, and also differential stretch-activated calcium channel signalling. Some of them may take place within minutes from the starting point of a therapeutic manoeuvre (Langevin et al., 2013). This article titled ‘cellular control of connective tissue matrix tension’ reviews the evidence supporting possible mechanisms underlying the response including ‘autocrine purinergic signalling’ and fibroblast regulation of connective tissue tension with respect to lymphatic flow, immune function and cancer. This review proposed that areolar “loose” connective tissue functions under normal physiological conditions as an “adjustable sponge”. This article will give a comprehensive idea about the in-vitro findings in cellular mechanisms but take reader to a positive bias by exploring only the positive findings without mentioning any of the negative findings or limitations of the studies they have reviewed. In a similar review, Ciobanasu et al. (2013) stated that fibroblasts could remodel their cell-matrix contacts (focal adhesions) along the direction of tissue stretch. Again these are inferences reached from limited in-vitro studies in this field super integrated with theoretical assumptions, not a confirmatory conclusion to ascertain that the cellular mechanism exactly functions in this way.

Tensional load appears to be perceived by the cell at a nuclear level too. Ex-vivo and in-vivo studies demonstrated that fibroblasts respond within minutes to mechanical stretching by actively remodelling their cytoskeleton with perinuclear redistribution of alpha-actin (Langevin et al., 2006; 2010). The ex-vivo study with subcutaneous tissue fibroblasts harvested from the abdomen of either mice or Wistar rats immediately after their death. They were dissected, fixed with suitable agents and stretched between stainless steel grips and elongated at a rate of 1 mm/s. Controls without load were placed in grips as described above and incubated for 30 min without tissue elongation (Langevin et al., 2006). This study was first of its kind to

show the cellular changes to mechanical stress by emphasising  $\alpha$ - and  $\beta$ -actin role in cellular mechanotransduction mechanisms. Even though these findings cannot be integratable to the properties of fascia in living beings, the findings can be used to explain the possible cellular changes during MFR. In the second study, Langevin et al. (2010) have hypothesised that tissue stretch would cause nuclear remodelling with a reduced amount of nuclear invagination, measurable as a change in nuclear concavity. They have taken subcutaneous areolar connective tissue samples from 28 mice and then randomised to either tissue stretch or no stretch for 30 minutes, then examined with histochemistry and confocal microscopy. In stretched tissue (vs. non-stretched), fibroblast nuclei had a larger cross sectional area ( $p < .001$ ), smaller thickness ( $p < .03$ ) in the plane of the tissue, and smaller relative concavity ( $p < .005$ ) indicating an increase in nuclear convexity, thus accepting the alternative hypothesis. The authors argued that the stretch-induced loss of invaginations may have important influences on gene expression, RNA trafficking and/or cell differentiation. This study has to be appreciated for its adherence to randomisation protocols and scientifically solid design. Although this property of rapidly responding to mechanical stress appears to be specific to areolar connective tissues only, it remains significant for fascial work because loose connective tissues form the interface between subcutaneous and perimuscular layers and are potentially engaged in manual interventions (Tozzi, 2015b).

#### **1.4.1. c. Possible Cellular Mechanisms**

Appropriate mechanical loading stimulates protein synthesis at the cellular level, promoting tissue repair and remodelling (Wang et al., 2012) as well as cell proliferation and migration in wound healing, by sensitizing fibroblasts to nitric oxide (Cao et al., 2013b)

During manual fascial techniques, the operator may feel various tissue responses to the applied load that are described as ‘resistance’ or ‘give’ to the stretch. Interestingly, the



mechanical loading of fascia causes changes through activation of fibroblast response and the different receptors present in the fascial tissue, leading to modulation of myofascial contraction (Hicks et al., 2014).

The existence of  $\alpha$ -smooth muscle actin (ASMA) in human fascia was discussed in an article by Schleip et al. in 2005 and hypothesised that fascia can undergo spontaneous contractions to create a pre-stress in the collagen scaffold, while no quantitative immunohistochemical examination has yet been published for cells containing ASMA in normal fascial sheets, the existence of cells resembling smooth muscle cells was accidentally discovered by Staubesand (1997) in normal crural fascia and has been documented with electron microscopy. Since the crural fascia has a similar morphology to the lumbar fascia or to the muscular epimysial envelopes, it seems reasonable to extrapolate that the crural fascia is not the only fascial sheet with this property (Schleip et al., 2005). It, therefore, can be cautiously assumed that contractile cells are probably also present in other dense human fascial sheets as have already been found in tendons, ligaments and in the crural fascia.

Masood and Naylor (1994 a, b; 1995) reported that superficial and deep lumbar fascia from rats as well as from guinea pigs contracted in response to in-vitro application of the myofibroblast stimulant mepyramine as well as to the smooth muscle agonists adenosine and angiotensine II. Contractions started within several minutes and were in a dose dependent, reproducible and reversible manner. The smooth muscle relaxing substances nifedipine and EDTA (ethylene diamine tetra acetic acid) as well as the microtubule disrupting substance cytochalasin-D exhibited a relaxing effect. A relaxing response in porcine lumbar fascia to the substance glyceryltrinitrate (a nitric oxide donor and smooth muscle relaxant) has been reported by Schleip et al. (2004). Malata et al. (1994) found that mepyramine-induced contractions in rat subcutaneous fascia were enhanced by previous incubation with heparin. Using an immunohistochemical analysis of 39 tissue samples from the thoracolumbar fascia of

11 human donors (ages 19–76 years), Schleip et al. (2004) demonstrated the widespread presence of myofibroblasts in all samples, with an average density of 79 cells/mm<sup>2</sup> in this longitudinal sections. In-vitro experiments with human lumbar fascia by Yahia et al. (1993) reported that with a tissue strip of 1.5 mm x 1.0 mm x 30 mm, the maximal measured force increase during an isometric stretch was 1.5 N. If we hypothetically apply the same force ratio to whole fascial sheets in the human body, it seems clear that such fascial contractions could have substantial biomechanical influences (Schleip et al., 2006).

Cao et al (2013) conducted an in-vitro scratch wound strain model analysis to determine the effects of modeled myofascial release on fibroblast wound healing and to investigate the potential role of nitric oxide (NO) in mediating these responses. They found that fibroblasts that received repetitive motion strain (RMS) resulted in reduced wound closure rates (vs nonstrain,  $P < .05$ ), which were partially attenuated by a single dose of MFR. Fibroblasts and myofibroblasts are both highly responsive to magnitude (Cao et al., 2013; Hicks et al., 2014), direction, frequency and duration (Standley & Meltzer, 2008) of a therapeutic load and can regulate cell activity, proliferation or apoptosis (Meltzer et al., 2010), mainly by influencing ion conductance, gene expression and secretion of inflammatory mediators. In particular, the secretion of IL-6 and IL-1 by fibroblasts under equibiaxial stretch can exert powerful pro or anti-inflammatory responses, potentially leading towards beneficial or detrimental matrix remodelling and cell behaviour (Tsuzaki et al., 2003). A concomitant autocrine and paracrine release of ATP may also serve as a negative feedback mechanism to limit activation of destructive pathways (Tsuzaki et al., 2003) and all of these factors may influence the clinical efficacy of fascial treatment.

The fascial tissue may respond better to balanced and sustained stretch rather than intermittent and unequal loads, including apoptotic rate (Meltzer et al., 2010). The force and

duration of tension applied may also be relevant. It has been shown that high magnitude (therapeutic) load (from 9% to 12% elongation) can produce an upregulation of ECM proteins while increasing magnitude and duration (one to five minutes) loads induce cytokine and growth factors secretions (Cao et al., 2013). These results are consistent with those obtained by Yang et al. (2005) where large-magnitude loads caused pro-inflammatory responses and cyclic (0.5 Hz per 4 h), uniaxial and small-magnitude stretching produced anti-inflammatory reactions in human tendon fibroblasts. Similarly, brief, moderate amplitude (20-30% strain), static stretching of connective tissue in-vivo and ex-vivo has been shown to decrease TGF- $\beta$ 1 and collagen synthesis, thus preventing soft tissue adhesions (Bouffard et al., 2008).

In conclusion, brief, light/moderate, balanced, static or slow cyclic strains appropriately applied to fascia may be sensed at the cellular level and transduced in normalizing tissue structure and function (Tozzi 2015b).

The therapeutic loads applied differently with respect to tissue tension (that presumably corresponds to cell orientation) may produce different cell and tissue responses. Finally, secretion of IL-6 was significantly induced by 15 min of cyclic biaxial mechanical stretching after 4 and 8 h in human tendon fibroblasts, suggesting that inflammatory reactions following manual intervention may be partially caused by IL-6 secretion (Skuttek et al., 2001).

#### **1.4.1. d. Neuromuscular Interaction**

Fascial oriented work may produce beneficial effects by activating various receptors in the connective tissues that elicit a series of neuromuscular reflexes. According to Schleip's neurobiological model (2003), these types of events occur together with concomitant autonomic and viscoelastic changes, and are more likely to explain the fast tissue responses that a therapist perceives during fascial techniques.

Although the dermis is the first tissue to be loaded during manual treatment, evidence suggests that therapeutic effects such as inhibition on hypertonic muscle and presumably on the myofascial complex do not originate from mechanical stimulation of superficial cutaneous mechanoreceptors (Merkel, Meissner receptors) during manual therapy (Morelli et al., 1999). Similarly, deep receptors such as Golgi tendon organs mainly exist in the myofascia, joint capsules and myotendinous junctions and are unlikely to come into play during fascial treatment because they have a high threshold that makes them respond to strong and fast manual stimulus to which they quickly adapt (Pickar & Wheeler, 2001). This is why Golgi organs have been mostly implied as being involved in neurophysiological explanations that underlie the efficacy of spinal manipulation (Pickar, 2002) and not of fascial treatment. In contrast, Pacinian corpuscles are present in dense connective tissue and deep fascia (Benjamin, 2009) and tend to quickly adapt to stimuli, hence they respond better to rapid or intermittent compression and vibrations applied to the myofascia, myotendinous junctions and deep capsular layers. They are thought to respond to such stimuli by enhancing proprioceptive feedback and by maintaining muscle tone. The type of therapeutic force needed to activate Pacinian corpuscles may be applied in some manual interventions such as in high velocity manipulation or vibratory techniques (Tozzi2015a).

Finally, Ruffini's endings are mainly located in joint capsules and in the dense connective tissue including fascia (Yahia et al., 1992). They have a slow adaptation to the stimuli being applied and are thus generally sensitive to slow, sustained or rhythmic deep pressures and in particular to lateral (perpendicular) tissue stretches (Van der Wal, 2012). These kinds of forces are normally applied in most fascial techniques, such as myofascial release.

The classical nociceptive model, instead, proposes that indirect fascial techniques may modulate muscle tone and related fascial tension by decreasing mechanical stress and neural inputs (Van Buskirk, 1990). This may in turn reduce the activity of nociceptors and of the

correspondent facilitated spinal level that by neurological reflex may produce a consequent modulation of autonomic activity on blood and lymphatic flow. Finally, in response to the proprioceptive input, the central nervous system may change muscle tone, allowing the therapist to follow myofascial paths of least resistance until a palpable release is perceived (Minasny, 2009).

#### **1.4.1. e. Autonomic Influence**

Somatic dysfunction has been traditionally related to correspondent facilitated spinal levels and aberrant autonomic activity that in turn influences various visceral functions (Beal, 1985). Interestingly, autonomic adrenergic fibres have been found in fascia with a plausible major role on vasomotor control of intrafascial blood vessels (Tesarz et al., 2011). It has been suggested that therapeutic touch may produce stimulation of pressure-sensitive mechanoreceptors in the fascia (Ruffini's and interstitial receptors) followed by a parasympathetic response (Schleip, 2003). This in turn may induce a change in local vasodilatation and tissue viscosity, together with a lowered tonus of intrafascial smooth muscle cells, and such a response has been partially demonstrated.

Both massage therapy and myofascial osteopathic treatment have been shown to produce an increase in vagal efferent activity, as shown by changes in heart rate (Field et al., 2010) even in healthy subjects (Giles et al., 2013). A modulation of hypersympathetic activity may take place (Henley et al., 2008).

#### **1.4.1. f. Viscoelastic Changes**

Biological structures exhibit viscoelastic properties and responses under mechanical loads (Kucharova' et al., 2007) with significant changes depending on chronological age (Doubal & Klemra, 2002). Generally, the stronger and more rapidly that a load is applied to organic materials, the more rigidly will the tissue respond, up to the point when the elastic potential of tissues is exceeded and a plastic deformation occurs (Jager, 2005).

Traditionally, it has been suggested that most of the immediate tissue changes following manual fascial work may be the result of a colloidal change in the fascia, which means a transformation of the ground substance from a dense solid-like state (gel) to a more fluid (sol) state (Rolf, 1962). However, a 3D mathematical model for fascial deformation has rejected the idea that palpable sensations of tissue release following manual therapy may be due to plastic deformations of firm type of fascia, such as the fascia lata and plantar fascia, whereas this may be possible in thin and more elastic types of fasciae (Chaudhry et al., 2012).

Schleip's neurobiological model has instead proposed that following proprioceptive stimulation the Ruffini's endings and interstitial fascia mechanoreceptors may be involved in efferent control of the vasodilation and increase of plasma extravasation via autonomic activation (Schleip, 2003). This would initiate ECM viscosity changes. Nevertheless, there is evidence that a similar phenomenon may take place within minutes of a tensional load being applied and as the result of cell matrix- induced regulation of fluid flow that is independent of neurological activation. Langevin et al. (2011) have demonstrated that static tissue stretch of areolar connective tissue causes fibroblast cytoskeletal remodelling via activation of focal adhesion complexes and initiation signalling pathways.

This in turn leads to remodelling of the cell's focal adhesions and actomyosin activation that develops counter tension. The latter process allows surrounding tissue to relax further and achieve a lower level of resting tension. The fibroblasts can dynamically modulate the viscoelastic behaviour of areolar connective tissue through cytoskeletal mechanisms (Tozzi 2015b).

#### **1.4.1. g. Fluid Dynamics**

The flow of water in the ECM depends on the opposing forces between the osmotic pull of under-hydrated glycosaminoglycans and the active restraint of the tensioned collagenous network as the result of fibroblast activity. Therefore, as long as the tension in the matrix is

maintained by fibroblasts, water is prevented from entering the tissue. During the acute onset of inflammation, however, the matrix swells as inflammatory mediators disrupt the cell-matrix contacts, causing a drop in matrix tension and interstitial fluid pressure, and allowing water to be ‘sucked into’ the matrix (Reed et al.,2010). A therapeutic stretch lasting for a few minutes could then potentially un-restrain the matrix and promote transcapillary fluid flow and temporary matrix swelling. Fibroblasts, in turn, can either release their matrix contacts - resulting in a further drop of interstitial fluid pressure - or remodel the contractile cytoskeleton and adhesive matrix contacts, so as to develop a counter-tension sufficient to restore tension equilibrium (Langevin et al., 2013). This model would also fit with the fascial hydrodynamic response reported by Schleip et al. (2012). In response to mechanical stimuli, such as compression and stretch, fascia may exhibit a sponge-like behaviour, showing a squeezing and refilling response under the opposing forces of the restraint of collagen network and the osmotic pull of proteoglycans complex.

Interestingly, the fluid pressure might increase more during tangential oscillation (2-4 Hz) and perpendicular vibration (15-60 Hz) with respect to the fascial layer than during constant sliding or back-and-forth motion, as predicted by 3D mathematical modelling methods (Roman et al., 2013; Chaudhry et al., 2013). This would cause the flow to occur more around the edges of the area under manipulation - due to an increased pressure gradient - producing an enhanced lubrication and an improved sliding potential between fascial layers and muscle tissue. Thus, the use of vibratory and oscillatory techniques—and not just constant sliding motions—should be considered, especially when interstitial fluid dynamics need to be improved such as in the case of fibrotic tissue. Interstitial flow also induces fibroblast-to-myofibroblast differentiation as well as collagen alignment and fibroblast proliferation, playing an important role in fibrogenesis and tissue repair (Ng et al., 2005). Furthermore, it appears to affect intracellular processes (calcium signalling, protein secretion) and influence fibroblast

activities such as growth, proliferation, differentiation, alignment, adhesion and migration (Dan et al., 2010) including tissue morphogenesis, remodelling and embryonic development (Rutkowski and Swartz, 2007) through mechanisms such as direct shear stress, matrix-cell transduction and autologous gradient formation. Interstitial flow may also be enhanced by the interplay of calcium ion concentration and unbound water oscillations (Lee, 2008), whose respective electric and pressure gradients improve the transport of oxygenation and nutrients in the tissues. Since fluid flow in the ECM is likely to transport metabolic and messenger substances (Meert, 2013), it may indeed play a role in restoring homeostasis where it has been compromised. For instance, it could improve drainage of inflammatory mediators. So, decreasing chemical irritation and nociceptive stimuli to nerve endings, hence leading to a reset of aberrant reflexes underlying somatic dysfunction.

#### **1.4.2. Mechanical Model**

In other words, the effectiveness of MFR can be explained under two broad classifications: mechanical and neurophysiological (Schleip, 2003; Simmonds et al., 2012). Mechanical mechanisms of MFR include thixotropy (Schleip, 2003), piezoelectricity (O'Connell, 2003; Schleip, 2003), fascial adhesions (Hedley, 2010; Martinez Rodriguez & Galandel Rí'o, 2013), cellular responses (Tozzi, 2012), fluid flow (Chaitow, 2009; Schleip & Muller, 2013), fascial inflammation (Bednar et al., 1995; Findley et al., 2012) and myofascial trigger points (Gerwin, 2010; Bron and Dommerholt, 2012). Many of these mechanical mechanisms have been criticized on the basis that pressures outside of normal human physiological ranges would be required in order to induce tissue deformations in most tissues (Chaudhry et al., 2008).

##### **1.4.2. a. Piezoelectric Model**

In the piezoelectric model, it is suggested that fibroblasts and fibroclasts, which create and digest the collagen fibres that are important for the biomechanical properties of the fascia,



respond to electric charges created through pressure (O'Connell, 2003). While piezoelectric effects have been observed in collagen fibres for many years (Facade&Yasuda, 1964), it has been argued that they cannot explain the quick effects that clinicians observe (Schleip, 2003) which typically occur within 90-120 seconds (Barnes, 1997). In the fascial adhesions model, it is suggested that different fascial layers that would normally slide relative to each other alter such that they now stick to one another (Hedley, 2010; Martinez Rodriguez & Galandel R10, 2013). These fascial adhesions are thought to be released by moving the body part through a full ROM under traction (Hedley, 2010). A detailed explanation of the piezoelectric model is presented in page 32; Session 1.3.1. i.

#### **1.4.2. f. Myofascial Trigger Points**

Myofascial Trigger Points (MTrPs) are discrete and hyperirritable nodule in a taut band of skeletal muscle which is palpable and tender during physical examination (Shah et al., 2015). An active MTrP is clinically associated with spontaneous pain in the immediate surrounding tissue and/or to distant sites in specific referred pain patterns. Strong digital pressure on the active MTrP exacerbates the patient's spontaneous pain complaint and mimics the patient's familiar pain experience. MTrPs can also be classified as latent, in which case the MTrP is physically present but not associated with a spontaneous pain complaint. However, pressure on the latent MTrP elicits local pain at the site of the nodule. Both latent and active MTrPs can be associated with muscle dysfunction, muscle weakness and a limited range of motion (Shah et al., 2015).

In a survey conducted in 2000, the vast majority of American Pain Society members believed MPS to be a distinct clinical entity characterized by the finding of MTrPs (Harden et al., 2000). By applying the clinical criteria developed by Travell and Simons (1999), the diagnosis of myofascial pain has historically relied heavily on the clinical history and a careful physical examination of the soft tissue by a trained clinician. Sikdar et al. (2009) reported local

milieu, as well as the nature of the tissue and whether its classification as pliable, stiff, homogeneous or nodular may be important for evaluation and treatment response.

The Cinderella Hypothesis (Hägg et al., 1991) provides a possible explanation for the role of muscle in MTrP development. This hypothesis describes how musculoskeletal disorder symptoms may arise from muscle recruitment patterns during sub-maximal level exertions with moderate or low physical load. According to Henneman's Size Principle, smaller type I muscle fibres are recruited first and de-recruited last during static muscle exertions. As a result, these “Cinderella” fibres are continuously activated and metabolically overloaded, in contrast to larger motor muscle fibres that do not work as hard and spend less time being activated. This property makes the “Cinderella” fibres more susceptible to muscle damage and calcium dysregulation, key factors in the formation of MTrPs (Shah & Gilliams, 2008). An observation study on sixteen female computer professionals by Treaster et al, (2006) demonstrated that low-level, continuous muscle contractions in office workers during 30 minutes of typing induced formation of MTrPs and thus supports the Cinderella Hypothesis. Though generalizability of a small observational study is often in question, this study gives a direction in which future scientifically and methodologically high quality trials can travel.

MTrPs can also develop as a result of muscle overuse in cervical and postural muscles during the performance of low-intensity activities of daily living and sedentary work (Treaster et al., 2006). An intriguing possible mechanism involves sustained low-level muscle contractions routinely used in tasks requiring precision and postural stability of the cervical spine and shoulder. As a result of sustained low-level contractions, a decrease in intramuscular perfusion has been postulated. Thus, it is conceivable that ischemia, hypoxia and insufficient ATP synthesis in type I motor unit fibres may occur and are responsible for increasing acidity,  $\text{Ca}^{2+}$  accumulation and subsequent sarcomere contracture. This increased and sustained sarcomere contracture may lead to decreased intramuscular perfusion, increased ischemia and

hypoxia, a vicious cycle that may possibly lead to the development of MTrPs. As a result, several sensitizing substances may be released, leading to local and referred pain in addition to muscle tenderness which are clinical hallmarks of MPS (Shah et al., 2015). Electromyographic studies have revealed spontaneous electrical activity (SEA) generated at MTrP loci that was not seen in surrounding tissue (Hubbard & Berkoff, 1993). Originally attributed to dysfunctional muscle spindles, the excess electrical activity was later identified as an increase in miniature endplate potentials and excessive acetylcholine (ACh) release (Hubbard & Berkoff, 1993). Using ultrasound imaging and elastography, Sikdar et al. (2009) in a small group (nine subjects) descriptive study demonstrated for the first time that there are abnormalities in the milieu of the muscle containing palpable MTrPs. They found nodular regions of hypoechogenicity on sonography.

In the presence of persistent nociceptive bombardment, the dorsal root ganglion will release 'substance P' and calcitonin gene-related peptide (CGRP) antidromically into the peripheral tissue. The peripheral secretion of these substances can lead to a cascade of events including the degranulation of local mast cells, local vasodilation, plasma extravasation and the development of a sensitizing biochemical soup. This process of 'neurogenic inflammation' leads to the enhanced release of endogenous substances, such as bradykinin, serotonin, norepinephrine, nerve growth factor and adenosine gradually leading to peripheral and central sensitization (Shah et al., 2015).

Whether muscle or fascia can alter pathologically in this way is unclear but there are indications that MFR and manual therapy in general can affect blood flow by increasing nitric oxide production (Quere' et al., 2009; Okamoto et al., 2014). Such fascial inflammation may be related to the concept of myofascial trigger points, which have been proposed to occur when motor endplates release excessive acetylcholine, shortening sarcomeres locally, disrupting cell membranes, damaging the sarcoplasmic reticulum and causing inflammation (Bron &

Dommerholt, 2012). However, the phenomenon of myofascial trigger points has been drawn into question by concerns over the reliability of their clinical identification (Myburgh et al., 2008) and conclusions drawn from low methodological quality studies.

### **1.4.3. Neurophysiological Model**

There are two main branches of neurophysiological mechanisms, one involving the Golgi reflex arc and another involving other mechanoreceptors.

#### **1.4.3. a. Golgi Reflex Arc Model**

In the Golgi reflex arc model, it is noted that Golgi receptors are found in all connective tissues, although they are only called Golgi tendon organs (GTOs) at the muscle-tendon junction. When a muscle is stretched, GTOs provide afferent feedback to the spinal cord. It is thought that pressure exerted during MFR might stimulate the GTOs, reduce motor unit firing rate and subsequently decrease muscle tension (Tozzi, 2012). However, it seems likely that muscles must be active in order for GTOs to be stimulated (Jami, 1992). It has been argued that this may be because the GTO is in series with the muscle (Schleip, 2003). During a passive stretch, the muscle likely absorbs most of the change in length of the muscle tendon unit whereas during an active stretch, this does not occur (Schleip, 2003).

#### **1.4.3. b. Mechanoreceptor Model**

The other main neurophysiological mechanism involves Ruffini and Pacini corpuscles and interstitial muscle receptors which are mechanoreceptors commonly found in fascia (Stecco et al., 2007a). Pressure applied to mechanoreceptors might stimulate the nervous system and thereby lead to reduced muscular tension (Schleip, 2003). Some investigations have shown that massage causes H-reflex inhibition (Morelli et al., 1999) which is an indirect measure of alpha motorneuron excitability. This phenomenon has also been attributed to the activation of mechanoreceptors, which are believed to inhibit the central nervous system during massage (Morelli et al., 1999).

### **1.4.3. c. Other Mechanisms**

In contrast to the above mechanisms that have traditionally been put forward to explain the effects of MFR, static stretching is thought to be effective primarily by means of its effects on stretch tolerance (Weppeler and Magnusson, 2010). It is possible that MFR may also prove to be effective through a similar mechanism, as manual therapies in general are typically reported as having a number of potentially pain-relieving effects (Bialosky et al., 2009; Voogt et al., 2015). Such analgesic effects have been described as being mediated by either peripheral, spinal, or supraspinal mechanisms (Bialosky et al., 2009). Peripheral mechanisms might involve the release of local inflammatory mediators (Bialosky et al., 2009). Spinal mechanisms could involve signals along large, primary afferent nerve fibres interfering with pain signals transmitted along slow-conducting, tertiary fibres.

These could then inhibit pain feedback in the spinal cord (Bialosky et al., 2009). Both peripheral and spinal mechanisms might be expected to occur based on the gate control theory of pain (Melzack, 1982). Supraspinal mechanisms are much less clear. Bialosky et al. (2009) suggested they might involve alterations in those parts of the brain responsible for the pain experience, such as the anterior cingulate cortex, the amygdala, periaqueductal gray and rostral ventromedial medulla. In whatever way they are affected, the analgesic effects that very likely arise following MFR could potentially produce an increase in stretch tolerance immediately following the application of the therapy, which could account for acute changes in flexibility. Although there has been substantial discussion of the potential mechanisms by which MFR might exert their effects, the research has until very recently been limited in respect of the acute and chronic clinical effects of MFR and self MFR (Beardsley & Škarabot, 2015).

Manual therapy theoretically restores mobility by re-optimizing the distribution of lines of force within fascia (Stecco et al., 2013; Day et al., 2009). Simulated myofascial release on in-vitro fibroblasts originally injured by repetitive motion strain results in normalization of cell

morphology and attenuation of inflammatory responses (Meltzer et al., 2010). There appears to be an important balance between the amount and type of strain resulting in cellular destruction and apoptosis versus cellular proliferation (Dodd et al., 2006; Meltzer et al., 2010). Recent studies have started to document immediate and delayed changes at the cellular level to manual treatments in-vivo (Crane et al., 2012).

Additionally, there have been theories regarding the myofascial connective tissue planes and acupuncture meridians (Langevin & Yandow, 2002). Acupuncture needles, with rotation, induce winding of connective tissue around the needle point (Langevin & Churchill, 2002). In-vitro models may be able to elucidate the response of acupuncture depending on the mechanostuctural characteristics such as collagen concentration and formation (Julias et al., 2008). Mechanical stimuli by acupuncture may induce remodeling of the extracellular matrix. Targeted remodeling may counteract any dysfunction in fascia. Further research is needed to identify how acupuncture helps treat myofascial pain at sites distant from the needle insertion (Kwong & Findley, 2014)

Further research is also needed about how fascia may be affected by other current treatment regimens such as therapeutic modalities, exercise, medications, interventional injections and surgery.

## **1.5. Fascia and Myofascial Release**

The fascial system consists of the three-dimensional continuum of soft, collagen containing, loose and dense fibrous connective tissues that permeate the body. It incorporates elements such as adipose tissue, adventitia and neurovascular sheaths, aponeuroses, deep and superficial fasciae, epineurium, joint capsules, ligaments, membranes, meninges, myofascial expansions, periosteum, retinacula, septa, tendons, visceral fasciae and all the intramuscular and intermuscular connective tissues including endo-/peri-/epimysium (Adstrum et al., 2017). The

fascial system interpenetrates and surrounds all organs, muscles, bones and nerve fibres, endowing the body with a functional structure, and providing an environment that enables all body systems to operate in an integrated manner (Adstrum et al., 2017). As fascia is able to modify its tensional state, strain transmission along the meridians might occur in response to changes of muscle activity. (Wilke et al., 2016). It not only lubricates the fibres but gives nourishment to all parts of the body. The fascial system is considered as a “tensegrity” or tensional integrity structure to manage the balance between tension and compression around the organs, joints and muscles (Chen et al., 2016). Repetitive mechanical straining of fibroblasts can also result in secretion of inflammatory mediators (Dodd et al., 2006). All of these changes could affect the normal functions of force transmission or sliding in the musculoskeletal system. This dysfunction could lead to pain or proprioceptive issues.

As fascia is able to modify its tensional state, strain transmission along the meridians might occur in response to changes of muscle activity. (Wilke et al., 2016). The central rule for the selection of a meridian’s components is a direct linear connection between two muscles. Myers (2014) defined eleven myofascial meridians connecting distant parts of the body by means of muscles and fascial tissues. Wilke et al. (2016), first showed that there is good evidence for the existence of three myofascial chains proposed by Myers (2009, 2014) through a systematic review. The results yielded strong evidence for myofascial transitions in three of the six examined myofascial meridians: Superficial back line, back functional line and front functional line. In the superficial back line there was moderate evidence for the meridians and transitions of the spiral line (five of nine verified transitions, based on twenty one studies) and the lateral line (two of five verified transitions, based on ten studies). Because fascia can transmit tension (Norton-Old et al., 2013) and in view of its proprioceptive and nociceptive functions, existence of myofascial meridians could be responsible for disorders and pain radiating to remote anatomic structures (Myers, 2009).

Myofascial release (MFR) is a form of manual therapy which involves the application of a low load, long duration stretch to the myofascial complex, intended to restore optimal length, decrease pain and improve function (Barnes, 1990). MFR is being used to treat patients with a wide variety of conditions, but there is scarcity of evidence to support its efficacy.

The effects of manual fascial interventions can be local (as tissue texture changes), segmental (as via neurological response) and global (as through hormonal effects) in extent, and may occur at different intervals—ranging from minutes to weeks—after a given input, with many interacting mechanisms influencing tissue properties and behaviours, including placebo. Some of these factors are strongly supported by the available evidence whereas others need further investigation (Tozzi, 2015b).

Three main manual approaches that are directed towards the fascia: i) direct approach - the affected tissue is brought against the restrictive barrier, described as a functional limit that abnormally diminishes the normal physiologic range (E.C.O.P., 2011a). This is maintained until tensions modify; ii) indirect approach - tissues are brought away from the restrictive barrier while a position of ease is found and maintained up to a release; iii) combined approach - both the point of ease and the restrictive barrier are consecutively engaged in an interactive fashion (Ward, 2003). Direct technique MFR is thought to work directly on restricted fascia; practitioners use knuckles or elbow or other tools to slowly sink into the fascia, and the pressure applied is a few kilograms of force (up to four kilograms) to contact the restricted fascia, apply tension or stretch the fascia. Indirect MFR involves application of gentle stretch- the pressure applied is in a lower range (up to half a kilogram) and the hands tend to follow the direction of fascial restriction, hold the stretch, and allow the fascia to ‘unwind’ itself. The rationale for these techniques can be traced to various studies that investigated cellular, viscoelastic and neurological properties of the fascial tissue (Schleip, 2014; Tozzi, 2015a, b). Fascial therapies



theoretically restores mobility by re-optimizing the distribution of lines of force within the fascia (Stecco et al., 2013; Day et al., 2009).

## **1.6. Objective of this Study**

To critically analyse three published randomised controlled trials (RCTs) and one systematic review on the effectiveness of myofascial release in various conditions.

## **1.7. Need and Significance of the Study**

MFR is being used to treat patients with a wide variety of conditions. But there is a lack of evidence to support its efficacy. Studies are emerging in this field with varying results and conclusions. Analysis of the recent research trials and reviews will be a better way to appraise the quality and reliability of such work. This work attempts to critically analyse three published randomised controlled trials (RCTs) and one systematic review on the effectiveness of myofascial release on various conditions with an aim of facilitating the creation of a more homogenous and reputable base for future trials in the field. A critical appraisal of the conducted studies and reviews to pin point this strengths and weaknesses can help to fine tune future studies. This type of approach and its findings can be highly useful for a manual therapy technique having lots of practice variations and applicability to set more controlled and methodologically superior studies in the future.

## Chapter 2

### Methodology at a Glance

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- 2.1. *Methodology at a Glance*
- 2.2. *Outcome Measures*
- 2.3. *Structure of the Thesis*

## Chapter 2

### Methodology at a Glance

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#### 2.1. Methodology at a Glance

This work attempts to critically analyse three published randomised controlled trials (RCTs) and one systematic review on the effectiveness of myofascial release on various conditions with an aim to facilitate in creating a respectable base for future trials in the field.

Three published randomised controlled trials (RCTs) and a systematic review on the effectiveness of MFR during the period of 2010 to 2015 were selected and analysed. The three RCTs selected were primarily evaluating the effectiveness of MFR on tension type headache (TTH), lateral epicondylitis (LE) and chronic low back pain (CLBP). The RCTs were analysed under subheadings like article title, technical details, synopsis, need and significance of the study, the principal research question and answer to it, demographic and methodological characteristics, risk of bias analysis, major findings, limitations and implications of the study. A conclusion was drawn at the end of each analysis

The systematic review was a comprehensive analysis of all the published RCTs in the MFR field till 2014. The systematic review was reviewed under the headings of criteria of selection, data analysis process, data synthesis and review of randomised controlled trials on Myofascial Release with a conclusion at the end. Since the three RCTs analysed here were already included in the systematic review, the in-depth analysis of the systematic review was merged with the thesis discussion part.

## **2.2. Outcome Measures**

The outcome measures used in this thesis to analyse the quality and level of evidence were the PEDro Scale and the Centre for Evidence-Based Medicine's (CEBM's) Levels of Evidence Scale. Additionally, a risk of bias analysis was included in the analysis of the RCTs and AMSTAR 2 tool was used to grade the quality of systematic review.

### **2.2. a. PEDro Scale**

Although there are many scales which are used to assess the quality of clinical trials, the 'PEDro Scale' is commonly employed in rating researches in the physiotherapy area (Maher et al., 2003). The PEDro Scale (Table 2.1) assesses methodological quality and consists of a checklist of 11 criteria, 10 of which are scored. For each criterion the study met, one point was awarded. The points were tallied and presented as a score out of 10. The scale applies only to experimental studies. The PEDro Scale considers two aspects of trial quality, the "internal validity" of the trial and whether the trial contains sufficient statistical information to make it interpretable. It does not rate the "meaningfulness", "generalisability" or "external validity" of the trial, or the size of the treatment effect. To assess the "internal validity" criteria, including random allocation, concealment of allocation, comparability of groups at baseline, blinding of patients, therapists and assessors, analysis by intention to treat and adequacy of follow-up were checked. Interpretability was measured by taking between-group statistical comparisons and reports of both point estimates and measures of variability. Trials are rated on the basis of what they report. If a trial does not report that a particular criterion was met, it will be scored as the criterion was not met. For this review, investigations with PEDro scores of 6-10 were considered high quality, of 4-5 were considered moderate quality, and of 0-3 were considered low quality (McKenney et al., 2013). The PEDro Scale does not evaluate clinical usefulness. In the past few years the PEDro Scale has undergone substantial psychometric validation (Maher et al., 2003; Bhogal et al., 2005; Foley et al., 2006; de Morton, 2009) and many

systematic reviews use it to rate the quality of the trials they include. Maher et al, (2003) reported an inter-rater reliability generalised kappa statistic of between 0.4 and 0.8 for the PEDro Scale which is in an acceptable range at individual item level and in total PEDro scores (Foley et al., 2006). The results of Rasch analysis indicated that the PEDro Scale measures only one construct – the methodological quality of clinical trials. Since there was no redundancy of PEDro Scale items, it is valid to combine PEDro item scores to obtain a total PEDro score as an indicator of methodological quality. Furthermore, the finding that there were no redundant items amongst the 10 PEDro Scale items, suggests that the PEDro Scale assesses a reasonable breadth of methodological quality. Clinicians and researchers can therefore confidently use the PEDro Scale to assess the methodological quality of clinical trials of physiotherapy interventions (de Morton, 2009).

**Table 2.1. Physiotherapy Evidence Database (PEDro) Scale**

<b>Item</b>	<b>Criteria</b>
<b>1</b>	Eligibility criteria were specified (no points awarded)
<b>2</b>	Subjects were randomly allocated to groups
<b>3</b>	Allocation was concealed
<b>4</b>	The groups were similar at baseline regarding the most important prognostic indicators
<b>5</b>	There was blinding of all subjects
<b>6</b>	There was blinding of all therapists who administered the therapy
<b>7</b>	There was blinding of all assessors who measured at least one key outcome
<b>8</b>	Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups
<b>9</b>	All subjects for whom outcome measures were available received the treatment or control condition as allocated

<b>10</b>	The result of between-group comparisons are reported for at least one key outcome
<b>11</b>	The study provides both point measures and measures of variability for at least one key outcome
<b>TOTAL</b>	Sum of scores for items 2-11

Since it is developed to assess the quality of the physiotherapy studies, the scale contains physiotherapy oriented components like the therapist and subject blinding. Unlike in drug trials, both therapist blinding and subject blinding are difficult to achieve in complex intervention trials. In most clinical trials of physiotherapy intervention, it is not possible to blind the therapist providing the intervention. Similarly, it is also difficult to blind participants to the physiotherapy intervention that they are receiving except in trials of electrotherapeutic interventions. One can say that PEDro Scale gives better methodological details of physiotherapy researches.

In 2005, Bhogal et al. systematically compared the PEDro Scale and the Jadad scale by applying to the stroke rehabilitation literature and concluded that the PEDro Scale provides more comprehensive measure of methodological quality in this field. The authors stated that in rehabilitation research, where double-blinding studies are often not possible due to the nature of the interventions, breaking down the levels of blinding and accounting for concealed allocation, intention-to-treat and attrition could be important and PEDro Scale is able to provide that.

In conclusion, the PEDro Scale is a reliable and valid measure of methodological quality of clinical trials with specific details that are main concerns of physiotherapy researches. Its items were ranked hierarchically from the least to the most adhered to item without redundancy. Since there was a high correlation between original PEDro ordinal scores

and transformed PEDro interval scores, PEDro data can be treated as interval level measurement. These findings support the use of the PEDro Scale for assessing the methodological quality of clinical trials (Maher et al., 2003; de Morton, 2009; Elkins et al., 2013)

## **2.2. b. The CEBM Levels of Evidence Scale**

In 1999, the Oxford Centre for Evidence-Based Medicine (OCEBM) developed a grading guideline to serve the needs of its junior medical staff (Atkins et al., 2004) with adaptations from other guidelines, notably from Canadian Task Force on Preventive Health Care (CTFPHE) and the Australian National Health and Medical Research Council (ANHMRC), and expanded the number of levels of evidence to five, including numerous sublevels. However, unlike previous guidelines, the OCEBM also developed a method for adjusting the level of evidence based on the quality with which the study was conducted (Gugiu & Gugiu, 2010).

The CEBM Levels of Evidence Scale (Phillips et al., 2009) (Table 2.2) assesses quality based on study design. Systemic reviews with homogeneity of RCTs are ranked in the highest levels while expert opinions rank the least. In both scales, RCTs receive higher rankings, particularly with long-term follow-up and narrow confidence intervals. Finding the levels of evidence is an important component of evidence based practice. Understanding the levels and why they are assigned to publications and abstracts helps the reader to prioritize information. The levels of evidence provide a guide and the reader needs to be cautious when interpreting these results (Burns et al., 2011). Bhandari et al. (2004) concluded that epidemiology and non-epidemiology-trained reviewers can apply the levels of-evidence to published studies with acceptable inter-observer agreement. The CEBM Scale is a simple and fast way to categorise the research publications so that both readers and investigators can use the logic of selecting the best evidences (McKeon et al., 2006; Medina et al., 2006).

<b>Table 2.2. Centre of Evidence-based Medicine: Levels of Evidence</b>	
<b>Level</b>	<b>Definition</b>
<b>1a</b>	Systematic reviews of randomised controlled trials
<b>1b</b>	Individual randomised controlled trial
<b>1c</b>	All-or-none studies
<b>2a</b>	Systematic reviews of cohort studies
<b>2b</b>	Individual cohort studies or low-quality randomised controlled trials
<b>2c</b>	Outcomes research
<b>3a</b>	Systematic reviews of case-control studies
<b>3b</b>	Individual case-control studies
<b>4</b>	Case series, poorly designed cohort or case-control studies
<b>5</b>	Animal and bench research, expert opinion

### **2.2.c. Risk of Bias Tool**

A bias is a systematic error or deviation from the truth in results or inferences. Biases can operate in either direction: different biases can lead to underestimation or overestimation of the true intervention effect. Biases can vary in magnitude: some are small (and trivial compared with the observed effect) and some are substantial (so that an apparent finding may be entirely due to bias). Differences in risks of bias can help explain variation in the results of the studies included in a systematic review. It is important to assess risk of bias in all studies in a review irrespective of the anticipated variability in either the results or the validity of the included studies.

The Cochrane 'Risk of Bias tool (RoB) is one of the most widely used tools for assessing the risk of bias (RoB) of clinical trials (Xy et al., 2016). The Risk of Bias tool covers six domains of bias: selection bias, performance bias, detection bias, attrition bias, reporting bias



and other bias. Within each domain, assessments are made for one or more items, which may cover different aspects of the domain or different outcomes (Table 2.3). The Risk of Bias tool is one of the most comprehensive approaches to assessing the potential for bias in randomised trials included in systematic reviews or meta-analyses. Inclusion of details of trial conduct, on which judgments of risk of bias are based, provides greater transparency than previous approaches, allowing readers to decide whether they agree with the judgments made. There are continuing uncertainty and great variation in practice over how to assess potential for bias in specific domains within trials, how to summarise bias assessments across such domains and how to incorporate bias assessments into meta-analyses (Higgins et al.,2011).

<b>Table 2.3. Cochrane Risk of Bias Assessment</b>			
<b>Bias domain</b>	<b>Source of bias</b>	<b>Support for judgment</b>	<b>Review authors' judgment (assess as low, unclear or high risk of bias)</b>
<b>Selection bias</b>	Random sequence generation	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence
	Allocation concealment	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen before or during enrolment	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations before assignment

<b>Performance bias</b>	Blinding of participants and personnel*	Describe all measures used, if any, to blind trial participants and researchers from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
<b>Detection bias</b>	Blinding of outcome assessment*	Describe all measures used, if any, to blind outcome assessment from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Detection bias due to knowledge of the allocated interventions by outcome assessment
<b>Attrition bias</b>	Incomplete outcome data*	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomised participants), reasons for attrition or	Attrition bias due to amount, nature, or handling of incomplete outcome data

		exclusions where reported, and any reinclusions in analyses for the review	
<b>Reporting bias</b>	Selective reporting	State how selective outcome reporting was examined and what was found	Reporting bias due to selective outcome reporting
<b>Other bias</b>	Anything else, ideally pre-specified	State any important concerns about bias not covered in the other domains in the tool	Bias due to problems not covered elsewhere

*\*Assessments should be made for each main outcome or class of outcomes.*

A recent study has found that the tool takes longer to complete than other tools (the investigators took a mean of 8.8 minutes per person for a single predetermined outcome using our tool compared with 1.5 minutes for a previous rating scale for quality of reporting) (Hartling et al., 2009). The reliability of the tool has not been extensively studied, although the same authors observed that larger effect sizes were observed on average in studies rated as at high risk of bias compared with studies at low risk of bias (Hartling et al., 2009). By explicitly incorporating judgments into the tool, one can acknowledge that the agreements between assessors may not be as high as for some other tools. However, we also explicitly target the risk of bias rather than reported characteristics of the trial. It would be easier to assess whether a drop-out rate exceeds 20% than whether a drop-out rate of 21% introduces an important risk of bias, but there is no guarantee that results from a study with a drop-out rate lower than 20% are at low risk of bias. Preliminary evidence suggests that incomplete outcome data and selective reporting are the most difficult items to assess; kappa measures of agreement of 0.32 (fair) and 0.13 (slight) respectively have been reported for these (Hartling et al., 2009).

The widespread adoption and implementation of the Risk of Bias tool, both within and outside the Cochrane Collaboration, will facilitate improved appraisal of evidence by healthcare decision makers and patients and ultimately lead to better healthcare. Improved understanding of the ways in which flaws in trial conducted may bias their results should also lead to better trials and more reliable evidence. Risk of bias assessments should continue to evolve, taking into account any new empirical evidence and the practical experience of authors of systematic reviews (Higgins et al., 2011). The Cochrane Risk of Bias tool for randomised clinical trials was introduced in 2008 and has frequently been commented on and used in systematic reviews. Jørgensen et al. (2016) have concluded that the Cochrane RoB tool has become the standard approach to assess risk of bias in randomised clinical trials but is frequently implemented in a non-recommended way.

#### **2.2. d. AMSTAR 2**

AMSTAR is a popular instrument for critically appraising systematic reviews of randomised controlled clinical trials. The revised instrument (AMSTAR 2) retains 10 of the original domains, has 16 items in total (compared with 11 in the original), has simpler response categories than the original AMSTAR, includes a more comprehensive user guide and has an overall rating based on weaknesses in critical domains (Appendix 10.5).

AMSTAR 2 is a major revision of the original AMSTAR instrument, which was designed to appraise systematic reviews that included randomised controlled trials (Shea et al., 2009). The main modifications include simplified response categories; a more detailed consideration of risk of bias with included studies, better alignment with the PICO (P – patient, problem or population; I – intervention; C – comparison, control or comparator; O – outcome) framework for research questions; a more detailed justification of selection of study designs for inclusion in a review; and more information on studies that were excluded from reviews. In

addition, emphasize on defining critical domains before starting an appraisal of a systematic review. Identification of weaknesses in these domains should undermine confidence in the results of a systematic review.

The responses to AMSTAR 2 items should not be used to derive an overall score (Greenland & O'Rourke, 2001). An overall score may disguise critical weaknesses that should diminish confidence in the results of a systematic review and AMSTAR 2 allows the users to adopt the rating process based on identification of critical domains or some variation based on these principles (Juni et al., 1999).

The consideration of risk of bias in individual studies is equally important for randomised and non-randomised studies of healthcare interventions but is generally better understood with the former. Large non-randomised studies, often conducted in large administrative databases, are increasingly being used to assess the real-world impact of a wide range of healthcare technologies and practices. Although such studies often use sophisticated methods, residual confounding or failure to deal with other sources of bias may lead to inaccurate estimates of effect. Inclusion of large observational studies in meta-analyses may generate precise but biased estimates of intervention effects (Egger et al., 1998). The items in AMSTAR 2 that deal with risk of bias identify domains specified in the Cochrane risk of bias instruments for randomised and non-randomised studies (Sterne et al., 2016). However, AMSTAR 2 does not currently specify which risk of bias instruments review authors should have used to assess non-randomised studies included in a systematic review. AMSTAR 2, as a critical appraisal instrument for systematic reviews, joins several published instruments designed for this purpose (Shea et al., 2017).

AMSTAR 2 provides a broad assessment of quality, including flaws that may have arisen through poor conduct of the review. In this respect it differs from the other instrument of this category, the 'Risk Of Bias In Systematic reviews' (ROBIS), which focuses more on

the risk of biases (Whiting et al., 2016). AMSTAR 2 is intended to be used for reviews of healthcare interventions. There is overlap in the items considered by ROBIS and AMSTAR 2; indeed, same investigators were involved in the development of both.

AMSTAR 2 is intended to be used for reviews of healthcare interventions. In its development, ten domains were retained from the original validated tool, albeit with some wording changes based on feedback and extensive experience of using it. Two domains were given more detailed coverage: duplicate study selection and data extraction now have their own items. An additional, more detailed and separate risk of bias for randomised and non-randomised studies are there. In total, four domains were added. Two of these come directly from the ROBINS-I.

The levels of agreement achieved by the three pairs of raters varied across items, but they were moderate to substantial for most items. Notably, the agreement between two raters involved in the development of AMSTAR 2 was no higher than that achieved by experienced raters who had not been involved its development. The average completion time ranges from 15-32 minutes.

The inter-rater reliability of AMSTAR 2 was measured with three pairs of raters and three sets of systematic reviews. The values varied substantially across items and between pairs of raters. Most values were in an acceptable range, with 46 of the 50  $\kappa$  scores falling in the range of moderate or better agreement and 39 displaying good or better agreement (Shea et al., 2017).

### 2.3. Structure of the Thesis

This thesis begins with Abstract, list of published works and statement of original authorship. The *Introduction* chapter has 7 sessions explaining Myofascial pain syndrome, defining myofascial release, fascia, MFR and myofascial dysfunction, objective of the study and need and significance of the study. The **second chapter** is **Methodology at a Glance** with sessions of outcome measures and structure of the thesis.

The **third to fifth chapters** explain the three RCTs analysed in this review-**tension head ache, lateral epicondylitis and chronic low back pain-** under various sub headings. They are title, link to journal abstract, technical details, synopsis, need and significance of the study, principal research question, demographic and methodological characteristics, risk of bias analysis, major findings of the study, answer to the principal research question, study limitations, Implications of the study with a conclusion at the end. The **sixth chapter** categorizes the selected **systematic review** for analysis under the sections review process, criteria of selection, data analysis process, data synthesis, other randomised controlled trials on MFR, AMSTAR analysis and conclusion.

The **seventh chapter** is prepared with an in-depth analysis of the three RCTs and one systematic review as the **discussion**. This is the prime focus of this thesis and analysed the **RCTs and systematic review** separately and in detail. The **eighth chapter** is the **conclusion** drawn from the analysis and contain the ending comment from the reviewers. The **references** and the **appendices** relevant to this thesis follows the eighth chapter.

## Chapter 3

### Direct vs Indirect Myofascial Release for Tension

### Headache

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- 3.1. *Online Title*
- 3.2. *Article Title*
- 3.3. *Link to Journal Abstract*
- 3.4. *Technical Details*
- 3.5. *Synopsis*
- 3.6. *Need and Significance of the Study*
- 3.7. *The Principal Research Question*
- 3.8. *Demographic and Methodological Characteristics*
- 3.9. *Risk of Bias Analysis*
- 3.10. *Major Findings of the Study*
- 3.11. *Answer to the Principal Research Question*
- 3.12. *Study Limitations*
- 3.13. *Implications of the Study*
- 3.14. *Conclusion*



## Chapter 3

# Direct vs Indirect Myofascial Release for Tension

## Headache

---

### 3.1. Online Title

Myofascial release in the management of tension type headache

### 3.2. Article Title

Effectiveness of direct vs indirect technique myofascial release in the management of tension type headache

### 3.3. Link to journal abstract

[http://www.bodyworkmovementtherapies.com/article/S1360-8592\(11\)00022-2/abstract](http://www.bodyworkmovementtherapies.com/article/S1360-8592(11)00022-2/abstract)

### 3.4. Technical details

#### 3.4.1. Journal

Journal of Bodywork & Movement  
Therapies

#### 3.4.2. Published date

October 2011

#### 3.4.3. Specialty 1

General Orthopaedics

#### 3.4.4. Specialty 2

Physical Therapy & Rehabilitation

#### 3.4.5. PMID#

21943616

#### 3.4.6. Type of Study

Interventional (Therapy)

**3.4.7. Quality of the study (PEDro)**

Moderate (6/10)

**3.4.9. All Authors**

M.S. Ajimsha

**3.4.8. Level of Evidence (CEBM)**

Level 2b Randomised controlled Trial

**3.4.10. Conflicts**

None disclosed

**3.5. Synopsis**

Tension-type headache (TTH) is essentially defined as bilateral headache of a pressing or tightening quality without a known medical cause. Myofascial release (MFR) is currently being applied for patients with TTH. But its efficacy was not been evaluated formally. Sixty three patients with episodic or chronic tension-type headache were given direct MFR technique, indirect MFR and a sham treatment and were compared. The study was of moderate quality (6/10) on PEDro with 2b level of evidence in CEBM Scale. The techniques were applied for 24 sessions per patient over 12 weeks with the difference in number of days with headache at baseline and post-test as the outcome measure. Patients in the direct MFR group, the indirect MFR group and the control group reported a 59.2%, 54% and 13.3% reduction respectively in their headache frequency in post-test compared to the baseline. The number of days with headache per four weeks decreased by 7.1 (2.6) [mean (SD)] days in the DT-MFR group compared with 6.7 (1.8) days in the IDT-MFR group and 1.6 (0.5) days in the control group ( $P < 0.001$ ). Patients in the DT-MFR group, IDT-MFR group and control group reported a 59.2%, 54% and 13.3% reduction in their headache frequency in weeks 17-20 compared to that in weeks 1-4. This study proved that direct technique or indirect technique MFR is more effective than the control intervention for tension headache. Lack of follow up, blinding of the therapists and the patient were the major limitations of the study.

### **3.6. Need and Significance of the Study**

A survey from the United States found a one-year prevalence of 38% for episodic tension-type headache and 2% for chronic tension-type headache (Schwartz et al., 1998). Present pain models for tension-type headache suggest that nociceptive inputs from peripheral tender muscles can lead to central sensitization in chronic tension-type headache (De-Las-Penas et al., 2007). Myofascial Trigger Points are highly prevalent in patients with tension-type headache (Couppe' et al., 2007). It has been hypothesized that fascial restrictions in one part of the body cause undue tension in other parts of the body, due to fascial continuity. In turn, this may create stress on any structures that are enveloped, divided or supported by fascia (Schleip et al., 2003). Myofascial practitioners believe that by restoring the length and health of restricted connective tissue, pressure can be relieved on pain sensitive structures such as nerves and blood vessels. Myofascial release (MFR) is currently being applied for patients with TTH but its efficacy has not been evaluated formally. The goal of the study was to investigate whether direct technique myofascial release (DT-MFR) reduces the frequency of headache more effectively than the indirect technique myofascial release (IDTMFR) in comparison to a control group receiving slow soft stroking.

### **3.7. The Principal Research Question**

Does direct technique myofascial release (DT-MFR) reduces the frequency of headache more effectively than the indirect technique myofascial release (IDTMFR) in comparison to a control group receiving slow soft stroking when assessed during weeks 1-4 and 17-20 of treatment?

## **3.8. Demographic and Methodological Characteristics**

### **3.8.1. Population**

Individuals aged 18-50 years with a diagnosis of episodic or chronic TTH lasting at least 12 months, and who had completed 4-week baseline headache diaries were included. Those with a history of additional migraine headache, secondary headaches, age >50 years, used analgesics on more than 10 days a month, had prophylactic headache treatment with drugs in the four weeks prior to randomization, and any other treatment for TTH during the previous 12 months were excluded. Between July 2008 and February 2009, 76 patients were referred to 'Myofascial therapy and research foundation', India, with a diagnosis of TTH. Of these, 63 individuals who met the inclusion criteria and provided written informed consent were randomised to DT-MFR, IDT-MFR, or control using a 2:2:1 list (Tully et al., 2007; Sherman et al., 2011).

### **3.8.2. Intervention**

All three interventions were provided twice weekly for 12 weeks (weeks 5-16); the duration of each treatment session was one hour. The technique used was the same for all the patients in (DT-MFR -Stanborough,2004; IDT-MFR- Manheim,2001). All techniques were performed bilaterally, 3 min on each side. (DT-MFR: Mean age: 43.7 +/- 5.6 n=24, 22 completed the study, 7M/15F; IDT-MFR: Mean age: 44.7 +/- 5.2, n=23, 22 completed the study, 8M/14F).

### **3.8.3. Comparison**

Patients in the control group received slow soft stroking with finger pads all over the head in the same areas as the application of MFR (in the other groups) for the same duration (1 h per treatment session), twice a week for 12 weeks. After the completion of the study, patients in the control arm were provided MFR therapy, as advised by the ethics committee. (Mean age: 43.0 +/- 5.4, n=13, 12 completed the study, 5M/7F).

### 3.8.4. Outcomes

Difference in numbers of days with headache between weeks 1-4 (i.e. four weeks prior to start of intervention) and weeks 17-20, following 12 weeks of intervention between weeks 5-16 as recorded by participants in headache diaries.

### 3.8.5. Time

Outcomes were assessed at baseline (weeks 1-4) and in week 17-20, following 12 weeks of intervention

## 3.9. Risk of Bias Analysis (Table 3.1)

<b>Bias</b>	<b>Authors' judgment</b>	<b>Support for judgment</b>
<b>Random sequence generation (selection bias)</b>	Low risk	Computer based randomisation using a 2:2:1 approach
<b>Allocation concealment (selection bias)</b>	Unclear risk	The randomisation list was created by a blinded statistician, but further description of allocation was not included
<b>Blinding of participants and researchers (performance bias)</b>	High risk	Participants and therapists were not blinded
<b>Blinding of outcome assessment (detection bias)</b>	Low risk	Two evaluators blinded to the group to which the participants belonged analyzed headache diaries

<b>Incomplete outcome data (attrition bias)</b>	High risk	Losses to follow-up were disclosed and were less than 5%  No sample size calculation mentioned
<b>Selective reporting (reporting bias)</b>	Low risk	All pre-specified outcomes were reported
<b>Other bias</b>	Low risk	Expertise of treating therapists including training and experience mentioned

### 3.10. Major Findings of the Study

3.10.1. There were no statistically significant differences between the groups for any of the baseline characteristics

3.10.2. From weeks 1-4 to weeks 17-20, the number of days with headache per four weeks decreased by 7.1 (SD 2.6) days in the DT-MFR group compared with 6.7 (SD 1.8) days in the IDT-MFR group and 1.6 (SD 0.5) days in the control group (difference: DT-MFR vs IDT-MFR, 0.6 days, 95% confidence interval -2.4 to 1.2 days, P=0.51; DT-MFR vs Control Group, 5.8 days, -7.6 to -4.0 days, P < 0.001, IDT-MFR vs Control Group, 5.4 days, -7.2 to -3.7 days, P < 0.001)

3.10.3. The proportion of responders, defined as participants who had at least 50% reduction in headache days between weeks 1-4 and weeks 17-20, was 81.8% in the DT-MFR Group, 86.4% in the IDT-MFR Group, and 0% in the control group.

3.10.4. Patients in the DT-MFR group reported a 59.2% reduction in their headache frequency; IDT-MFR group reported 54% reduction whereas control group reported 13.3% reduction in their pain frequency per four weeks in the weeks 17-20.

3.10.5. Differences in headache frequency between the DT-MFR and the IDT-MFR groups were statistically insignificant.

3.10.6. No serious adverse events occurred in any of three groups as a result of treatment.

3.10.7. Three patients from the DT-MFR group and one from the IDT-MFR group reported headaches in the first week following initiation of treatment and this was reported to have subsided within a week without any medication.

### **3.11. Answer to the Principal Research Question**

3.11.1. This study provides evidence that direct technique or indirect technique MFR is more effective than the control intervention for tension headache.

3.11.2. The proportion of responders, defined as participants who had at least 50% reduction in headache days between weeks 1-4 and weeks 17-20, was 81.8% in the DT-MFR group, 86.4% in the IDT-MFR group, and 0% in the control group.

### **3.12. Study Limitations**

Participants and treating physiotherapists were not blinded to the intervention they were randomised to. Another limitation was the absence of long-term follow up of study participants. A slight improvement over time occurred in the control group; this could be due to a “meaning response” (Moerman and Jonas, 2002).

### **3.13. Implications of the Study**

Prevalence of episodic/ chronic tension type headache is very high across the globe and directly influencing the burden of care. MFR can be a non-invasive, non-pharmacological and low cost alternative for its management. A significant proportion of patients with TTH might benefit from the use of MFR.

### 3.14. Conclusion

Both the direct and indirect techniques of MFR investigated in this trial were more effective than a control intervention consisting of slow soft stroking with finger pads for the treatment of tension-type head ache. A significant proportion of patients with TTH might benefit from the use of Myofascial Release. The mechanisms underlying these responses merit investigation.

**Table 3.2: Headache diary readings (17-20 weeks) following completion of three months intervention. Data are the means (SD).**

Headache diary reading	DTMFR	IDTMFR	Control group
Headache frequency (weeks 1-4)	12 (2.8)	12.4 (2.8)	12 (2.5)
Headache frequency (weeks 17-20)	4.9 (1.7)	5.7 (1.3)	10.4 (2.7)
Mean (SD) of difference in days with headache between weeks 1-4 and weeks 17-20	7.1 (2.6)	6.7 (1.8)	1.6 (0.5)
Comparison of headache frequency scores of the DTMFR, IDTMFR and the control groups of the weeks 17-20. (95% Confidence Interval)	DTMFR Vs IDTMFR	DTMFR Vs Control group	IDTMFR Vs Control Group
	-0.6 (-2.4 to 1.2)	-5.8 (-7.6 to -4.0)	-5.4 (-7.2 to -3.7)
<i>P value</i> by unpaired <i>t</i> -test	0.51	< 0.001	< 0.001



## Chapter 4

### Myofascial Release for Lateral Epicondylitis

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- 4.1. *Online Title*
- 4.2. *Article Title*
- 4.3. *Link to Journal Abstract*
- 4.4. *Technical Details*
- 4.5. *Synopsis*
- 4.6. *Need and Significance of the Study*
- 4.7. *The Principal Research Question*
- 4.8. *Demographic and Methodological Characteristics*
- 4.9. *Risk of Bias Analysis*
- 4.10. *Major Findings of the Study*
- 4.11. *Answer to the Principal Research Question*
- 4.12. *Study Limitations*
- 4.13. *Implications of the Study*
- 4.14. *Conclusion*

# Myofascial Release for Lateral Epicondylitis

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### 4.1. Online Title

Myofascial release as a treatment for lateral epicondylitis

### 4.2. Article Title

Effectiveness of Myofascial Release in the Management of Lateral Epicondylitis in Computer Professionals

### 4.3. Link to Journal Abstract

[http://www.archives-pmr.org/article/S0003-9993\(11\)00914-2/abstract](http://www.archives-pmr.org/article/S0003-9993(11)00914-2/abstract)

### 4.4. Technical details

#### 4.4.1. Journal

Archives of Physical Medicine &  
Rehabilitation

#### 4.4.2. Published date

April 2012

#### 4.4.3. Specialty 1

General Orthopaedics

#### 4.4.4. Specialty 2

Physical Therapy & Rehabilitation

#### 4.4.5. PMID#

22236639

#### 4.4.6. Type of study

Interventional (Therapy)

#### 4.4.7. Quality of the study (PEDro)

Moderate to high (7/10)

#### 4.4.8. Level of evidence (CEBM)

Level Ib- (Randomised controlled Trial)

#### 4.4.9. All authors

Ajimsha MS, Thulasyammal RP, ChithraS

#### 4.4.10. Conflicts

None disclosed

## **4.5. Synopsis**

The study investigated whether MFR reduces pain and functional disability of lateral epicondylitis (LE) in comparison with a control group receiving sham ultrasound therapy (SUST) in computer professionals (N = 68) for 12 sessions per client over four weeks with the Patient-Rated Tennis Elbow Evaluation (PRTEE) as the main outcome measure taken after the treatment (four weeks) and in follow up (12 weeks). The study was of a moderately high quality on the PEDro Scale (7/10) with 1b- level in CBEM. The MFR group performed better than the control group at weeks 4 and 12. Patients in the MFR and control groups reported a 78.7% and 6.8% reduction, respectively, in their pain and functional disability in week four compared with that in week one, which persisted as 63.1% in the follow-up at week 12 in the MFR group. Lack of therapist blinding was the major limitation of the study. A slight improvement over time occurred in the control group at week four and the authors are attributing this to a meaning response. This study provided evidence that MFR is more effective than a control intervention for LE in computer professionals.

## **4.6. Need and significance of the study**

Musculoskeletal complaints in the neck and upper extremity because of computer work are common in modern society and both show an increasing trend (Waersted et al., 2010). Lateral epicondylitis is characterized by pain in the external aspect of the elbow exacerbated during elbow extension with the wrist in flexion or by resisted extension of the wrist with the elbow in extension (Evans 2001). LE is the most commonly diagnosed elbow condition, affecting approximately 1% to 3% of the general population each year (Nirschl 1992; Verhaar 1994), with workplace activities contributing to 35% to 64% of all cases (Dimberg 1987). Myofascial release (MFR) is a form of manual therapy that involves the application of a low load and long duration stretch to the myofascial complex, with the intention of restoring length, decreasing pain, and improving function. MFR is being used to treat patients with LE, but there

are few formal reports of its efficacy. The goal of this study was to evaluate the efficacy of MFR in the management of LE in computer professionals, treating fascia in the extensor aspect of the forearm in accordance with the fascial meridians proposed by Myers (2009).

#### **4.7. The Principal Research Question**

Does myofascial release (MFR) reduce the pain and functional disability of lateral epicondylitis (LE) in comparison with a control group receiving sham ultrasound therapy in computer professionals after eight weeks of treatment with four week follow-up?

#### **4.8. Demographic and Methodological Characteristics**

##### **4.8.1. Population**

The sample included 68 computer professionals, aged 20 to 40 years with a diagnosis of LE on the mouse-operating arm based on the Southampton examination criteria for LE (Walker-Bone 2004; Palmer et al.,2007); pain lasting  $\geq 1$  day in the last 7 days in the lateral elbow region, tenderness over the lateral elbow region, and pain occurring over the lateral elbow region during resisted active extension of the wrist; pain lasting at least 3 months; those working with a personal computer, computer terminal or equivalent device with a computer mouse; those using a computer for 50% or more of the workday; and those who had completed a baseline PRTEE Scale (Overend et al.,1999). Those with a history of trauma to the affected elbow in the preceding 6 weeks, history of elbow instability, previous elbow surgery, any other pathology involving the affected upper limb or cervical spine, use of oral/systemic steroids, use of analgesics on more than 10 days a month and any other treatment for LE during the previous 6 months were excluded from the study.

#### **4.8.2. Intervention**

**MFR Group:** Patients received direct MFR treatment 3 times/week for four weeks, with a minimum of one day between sessions. All techniques were performed on the affected extremity for 30 minutes. The MFR procedure consisted of: i. treating from the common extensor tendon to the extensor retinaculum of the wrist (5min x 2 repetitions). ii. treating through the periosteum of the ulna (5min x 2 repetitions), iii. spreading the radius from the ulna (5min x 2 repetitions). (Details of protocol provided in full within the publication) (Mean age: 35.8 +/-8.4) (n=34, 33 completed final follow up, 13M/20F).

#### **4.8.3. Comparison**

**Control Group:** Patients in the control group received sham ultrasound therapy (SUST) over the extensor aspect of the forearm in the same 3 areas as the application of MFR (in the other group) for 30 minutes per treatment session (10min x 3areas), three times a week for four weeks. SUST units were prepared by removing the ultrasound producing quartz crystal from the treatment transducer head of the ultrasound therapy units. After the completion of the study, patients in the control arm were provided MFR therapy, as advised by the ethics committee. (Mean age: 29.3 +/- 4.9) (n=34, 32 completed final follow up, 14M/18F)

#### **4.8.4. Outcomes**

The Patient-Rated Tennis Elbow Evaluation (PRTEE) scale was used to assess pain severity and functional disability. The primary outcome measure was the difference in PRTEE scale scores between week one (pre-test score), week four (post-test score), and follow-up at week12 after randomization.

#### **4.8.5. Time**

Outcomes were assessed at baseline, four weeks, and follow-up at week12 after randomization.

#### 4.9. Risk of Bias Analysis (Table 4.1)

<b>Bias</b>	<b>Authors' judgment</b>	<b>Support for judgment</b>
<b>Random sequence generation (selection bias)</b>	Low risk	Computer generated randomisation
<b>Allocation concealment (selection bias)</b>	Unclear risk	The randomisation list was created at the blinded statistician, but further description of allocation is not included
<b>Blinding of participants and researchers (performance bias)</b>	High risk	Participants were blinded but the therapists were not blinded
<b>Blinding of outcome assessment (detection bias)</b>	Low risk	Two evaluators blinded to the group to which the participants belonged analyzed scores
<b>Incomplete outcome data (attrition bias)</b>	High risk	Losses to follow-up were disclosed and were less than 5%  No sample size calculation mentioned
<b>Selective reporting (reporting bias)</b>	Low risk	All pre-specified outcomes were reported
<b>Other bias</b>	Low risk	Expertise of treating therapists including training and experience mentioned

## 4.10. Major Findings of the Study

- 4.10.1. The mean differences between groups vary by time. This indicates the possible existence of their interaction effect
- 4.10.2. The patients in the MFR group reported a 78.7% reduction in their pain and functional disability as shown in the PRTEE scale score in week four, whereas patients in the control group reported a 6.8% reduction in their PRTEE scale score in week 4, which persisted as a 63.1% reduction in the follow-up at week 12 in the MFR group, whereas the control group showed a 2.2% increase in their symptoms during follow-up (week 12) in their PRTEE scale score.
- 4.10.3. The proportion of responders, defined as participants who had at least a 50% reduction in pain and functional disability between weeks 1 and 4, was 100% in the MFR group and 0% in the control group.
- 4.10.4. The simple main effects analysis showed that the MFR group significantly performed better than the control group in weeks 4 and 12 ( $P < .001$ ).
- 4.10.5. The interactions between time and group were significant based on univariate and multivariate methods for all repeated-measures ANOVAs. Significant pairs of MFR and control groups vary at weeks 4 and 12 due to the interaction effect between group type and time.
- 4.10.6. One participant from the MFR group and two from the control group dropped out of the study without providing any specific reason and their data were excluded from the results.
- 4.10.7. Within the study period, no serious adverse events occurred in either of the groups as recorded in the patient diary. Five patients from the MFR group reported an increase of pain in the first week after initiation of treatment, and this was reported to have subsided within a week without any medications.

#### **4.11. Answer to the Principal Research Question**

The simple main effects analysis showed that the MFR group performed better than the control group in weeks 4 and 12 ( $P < .005$ ). Patients in the MFR and control groups reported a 78.7% and 6.8% reduction, respectively, in their pain and functional disability in week four compared with that in week one, which persisted as 63.1% in the follow-up at week 12 in the MFR group.

#### **4.12. Study Limitations**

Practitioners in this trial could not be blinded. A slight improvement over time occurred in the control group at week four; this could be due to a meaning response.

#### **4.13. Implications of the Study**

The results of the study suggest that MFR is a beneficial tool for managing LE in computer professionals. This study was limited by a short follow up period, and very few outcome measurements. Future studies with larger sample sizes and longer follow up periods should be completed to verify these results.

#### **4.14. Conclusion**

The MFR investigated in this trial was more effective than a control intervention with SUST for the treatment of LE. A significant proportion of computer professionals with LE might benefit from the use of MFR. The mechanisms underlying these responses merit further investigation.



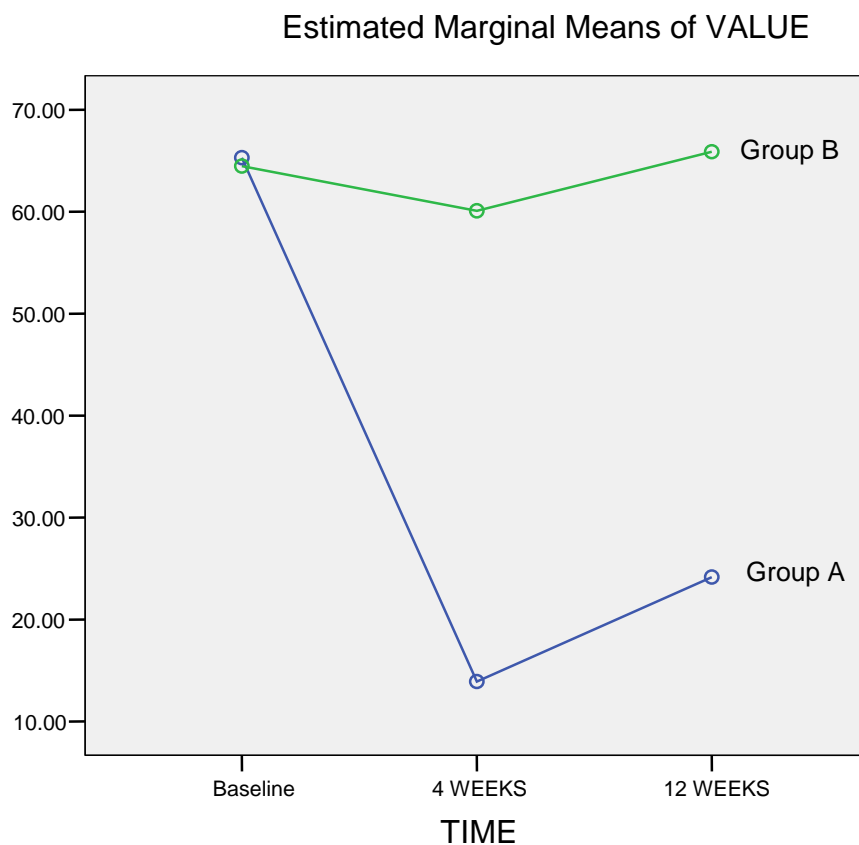
**Table 4.2: Pair-wise comparisons of group and time**

Time	Group I Group II	Mean Difference (I-J)	Std. Error	Sig. <sup>a</sup>	95% Confidence Interval for difference <sup>a</sup>
Baseline	MFR Control	.819	1.135	.472	-1.42 to 3.06
	MFR Control	-.819	1.135	.472	-3.06 to 1.42.
Week 4	MFR Control	-.46.185*	1.135	.000	-48.42 to -43.95
	MFR Control	.46.185*	1.135	.000	43.95 to 48.42
Week 12	MFR Control	-41.739*	1.135	.000	-43.98 to -39.5
	MFR Control	41.739*	1.135	.000	39.5 to 43.98

Based on estimated marginal means

\*The mean difference is significant at the .050 level

**Figure 4.1: Effects of group and time on value (Group A=MFR & Group B=Control)**



a. Adjustment for multiple comparisons: Least significant Difference (equivalent to no adjustment)

## Chapter 5

# Myofascial Release for Chronic Low Back Pain

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- 5.1 *Online Title*
- 5.1 *Article Title*
- 5.1 *Link to Journal Abstract*
- 5.1 *Technical Details*
- 5.1 *Synopsis*
- 5.1 *Need and Significance of the Study*
- 5.1 *The Principal Research Question*
- 5.1 *Demographic and Methodological Characteristics*
- 5.1 *Risk of Bias Analysis*
- 5.1 *Major Findings of the Study*
- 5.1 *Answer to the Principal Research Question*
- 5.1 *Study Limitations*
- 5.1 *Implications of the Study*
- 5.1 *Conclusion*

## Chapter 5

# Myofascial Release for Chronic Low Back Pain

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### 5.1. Online Title

Myofascial release as an adjunct to specific back exercise for chronic low back pain

### 5.2. Article Title

Effectiveness of Myofascial release in the management of chronic low back pain in nursing professionals

### 5.3. Link to Journal Abstract

[http://www.bodyworkmovementtherapies.com/article/S1360-8592\(13\)00074-0/abstract](http://www.bodyworkmovementtherapies.com/article/S1360-8592(13)00074-0/abstract)

### 5.4. Technical Details

#### 5.4.1. Journal

Journal of Bodywork & Movement  
Therapies

#### 5.4.2. Published date

April 2014

#### 5.4.3. Specialty 1

General Orthopaedics

#### 5.4.4. Specialty 2

Physical Therapy & Rehabilitation

#### 5.4.5. PMID#

24725797

#### 5.4.6. Type of study

Interventional (Therapy)

#### 5.4.7. Quality of the study (PEDro)

Moderate to high (7/10)

#### 5.4.8. Level of evidence (CEBM)

Level 1b Randomised controlled Trial

#### 5.4.9. All authors

Ajimsha MS, Daniel B, Chithra S

#### 5.4.10. Conflicts

None disclosed

## **5.5. Synopsis**

Eighty nursing professionals (aged 20 to 40 years) with chronic low back pain (CLBP) (pain for three or more months) were randomly assigned into one of two groups to determine if MFR effectively reduces CLBP. The study was a high quality one (PEDro score of 7/10 and CBEM level of 1b). The aim was to investigate whether MFR when used as an adjunct to specific back exercises (SBE) reduces pain and disability in CLBP in comparison with a control group receiving a sham MFR and SBE among nursing professionals. The McGill Pain Questionnaire (MPQ) was employed to assess subjective pain experience and Quebec Back Pain Disability Scale (QBPDS) was employed to evaluate the disability associated with CLBP. The primary outcome measure was the difference in MPQ and QBPDS scores between week one (pre-test score), week 8 (post-test score), and follow-up at week 12 after randomization. The patients in the MFR group reported a 53.3% diminution in their pain and 29.7% decrease in functional disability as evidenced in the MPQ and QBPDS scores in week 8, whereas patients in the control group reported a 26.1% and 9.8% decrease in their MPQ and QBPDS scores in week 8, which persisted as a 43.6% reduction of pain and 22.7% reduction of functional impairment in the follow-up at week 12 in the MFR group compared to the baseline. The proportion of participants responding to treatment (i.e. at least a 50% reduction in pain from week 1 to 8) was 73% in the MFR group and 0% in the control. No patient within the MFR or control groups exhibited a 50% reduction in functional disability within the first 8 weeks. The authors advocated examining other outcomes such as pain beliefs, mood, and quality of life in future studies.

## **5.6. Need and Significance of the Study**

Chronic Low Back Pain (CLBP) affects roughly 60% to 80% of the general population at some point in their lives (Maul et al., 2003). Work-related CLBP among nurses is suggested to be even more prevalent, estimated at 73% to 90% (Maul et al., 2003; Knibbe and Friele, 1996; Smedley

et al., 1995). Myofascial release (MFR) is a form of manual medicine that has become increasingly popular for patients with low back pain, although high-quality evidence on its efficacy remains scarce. The goal of this study was to determine if a direct MFR technique could effectively reduce back pain in nursing professionals with CLBP.

## **5.7. The Principal Research Question**

Does direct MFR, in combination with SBE, effectively reduce CLBP among nursing professionals in comparison to a sham treatment when assessed after 8 weeks of treatment with four weeks of follow-up?

## **5.8. Demographic and Methodological Characteristics**

### **5.8.1. Population**

Eighty nursing professionals, aged 20 to 40 years, diagnosed with CLBP (duration of 3 or more months), and who were judged to have musculoskeletal pain (based on evaluation by physician or physical therapist). All patients took part in SBE regardless of treatment allocation. The participants were educated on musculoskeletal pain and SBE with the help of an informational video.

### **5.8.2. Intervention**

MFR Group: Patients received direct MFR treatment 3 times/week for 8 weeks, with a minimum of one day between sessions. The duration of each treatment session was 60 min (40 min MFR and 20 min SBE). The MFR procedure consisted of: MFR of the lower thoracolumbar fasciae and gluteus maximus, MFR of the myofascia of the posterior hip & piriformis, lower back work in the prone position, pressure application while seated for the deeper muscles of the lower back, and fascia release of the trunk (Stanborough 2004) (details of protocol provided in full within the publication) (Mean age: 35.8 +/-8.4) (n=40, 38 completed final follow up, 9M/29F).

### 5.8.3. Comparison

SMFR (sham) Group: Patients in this group received sham MFR (SMFR) treatment 3times/week for 8 weeks, with a minimum of one day between sessions. The duration of each treatment session was 60 min (40 min SMFR and 20 min SBE). SMFR was applied to the same areas as the MFR group. The sham treatment was completed by gently placing a hand over the area that was to be treated but never applying enough pressure to elicit an effect (Mean age: 34.2 +/- 9.3) (n=40, 36completed final follow up, 8M/28F)

### 5.8.4. Outcomes

Outcome measures included the McGill Pain Questionnaire (MPQ) for pain (Melzack 1975) and Quebec Back Pain Disability Scale (QBPDS) score for functional disability (Kopeck et al., 2004).

### 5.8.5. Time

Outcomes were assessed at baseline, 8 weeks, and 12 weeks.

## 5.9. Risk of Bias Analysis (Table 5.1)

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	Computer generated randomisation
Allocation concealment (selection bias)	Unclear risk	The randomisation list was created by the blinded statistician, but further description of allocation was not included

<b>Blinding of participants and researchers (performance bias)</b>	High risk	Participants were blinded but the therapists were not blinded
<b>Blinding of outcome assessment (detection bias)</b>	Low risk	Two evaluators blinded to the group to which the participants belonged analyzed scores
<b>Incomplete outcome data (attrition bias)</b>	High risk	Losses to follow-up were disclosed and were less than 5%  No sample size calculation mentioned
<b>Selective reporting (reporting bias)</b>	Low risk	All pre-specified outcomes were reported
<b>Other bias</b>	Low risk	Expertise of treating therapists including training and experience mentioned

## 5.10. Major Findings of the Study

5.10.1. Patients in the MFR group reported a 53.3% reduction in pain and 29.7% reduction in functional disability at week 8, compared to 26.1% and 9.8% reduction in the control. These findings persisted at the 12 week follow up, with the MFR group experiencing a 43.6% reduction in pain and 22.7% reduction in functional disability, compared to 20.4% and 7.7% reduction in the SMFR group.

5.10.2. Proportion of participants who had at least a 50% reduction in pain between weeks 1 and 8 was 73% in the MFR group and 0% in the control. 0% of individuals in the MFR or control group experienced at least a 50% reduction in functional disability from week 1 to 8.

5.10.3. Two-way ANOVA testing demonstrated a significant interaction between the effects of group and time on MPQ and QBPDS values ( $p < 0.001$ ), and a simple main effects analysis indicated that the MFR group performed significantly better than the control group in the 8 and 12 week follow ups ( $p < 0.001$ ).

5.10.4. Ten patients in the MFR group and one from the control group reported an increase in pain after the first week of treatment. This finding subsided within a week where no medication was consumed by the participants.

5.10.5. No serious adverse events occurred in either group as a result of treatment.

### **5.11. Answer to the Principal Research Question**

A main effects analysis indicated that the MFR group performed better in all measured outcomes, at 8 and 12 week follow up, when compared to the control group. The proportion of participants who had at least a 50% reduction in pain between weeks 1 and 8 was 73% in the MFR group and 0% in the control. None of the individuals in the MFR and control group experienced at least a 50% reduction in functional disability from week 1 to 8.

### **5.12. Study Limitations**

One limitation of this trial was that practitioners could not be blinded. Second, long-term outcomes were not assessed, and it is not known whether the differences observed at post-treatment can be maintained over a long time. Other important treatment outcomes such as pain beliefs, mood and quality of life are not studied

### **5.13. Implications of the Study**

The results of the study suggest that MFR is a beneficial adjunct to SBE when treating nursing professionals with CLBP. This study was limited by a short follow up period, and very



few outcome measurements. Future studies with larger sample sizes and longer follow up periods should be completed to verify these results.

## 5.14. Conclusion

This study provides evidence that MFR when used as an adjunct to SBE is more effective than a control intervention for CLBP in nursing professionals. A significant proportion of nursing professionals with CLBP might benefit from the use of MFR. The mechanisms underlying these responses merit further investigation.

*Table 5.2: Pair-wise comparisons of group and time*

	Time	Group I	Group II	Mean Difference (Group I value – Group II value)	SE	P*
<b>MPQ</b>	Baseline	Control	MFR	1.000	0.548	<b>0.133</b>
	Week 8	Control	MFR	4.813 <sup>f</sup>	0.810	<b>0.000</b>
	Week 12	Control	MFR	3.250 <sup>f</sup>	0.624	<b>0.000</b>
<b>QBPDS</b>	Baseline	Control	MFR	0.971	0.435	<b>0.472</b>
	Week 8	Control	MFR	3.413 <sup>f</sup>	0.688	<b>0.000</b>
	Week 12	Control	MFR	2.023 <sup>f</sup>	0.532	<b>0.000</b>

NOTE: Based on estimated marginal means

\*Adjustment for multiple comparisons: least significant difference (equivalent to no adjustment)

\* The mean difference is significant at the .05 level

## **Chapter 6**

# **Systematic Review of Myofascial Release**

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- 6.1. Systematic Review of Myofascial Release**
- 6.2. Review Process**
- 6.3. Criteria of selection**
- 6.4. Data analysis process**
- 6.5. Data synthesis**
- 6.6. Randomised Controlled Trials on Myofascial Release:  
Others**
- 6.7. AMSTAR 2 analysis**
- 6.8. Conclusion**

## Chapter 6

# Systematic Review of Myofascial Release

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### 6.1. Systematic Review of Myofascial Release

The systematic review of the effectiveness of MFR included here was a comprehensive one, analysing most the MFR RCTs published in peer reviewed journals until 2014. An in-depth analysis of the published RCTs was done in succession. A total of nineteen RCTs covering 1228 patients were included in this systematic review. The sample size varied from 10 to 200 with an average of 65 (SD  $\pm$  42.68). The methodological qualities of the included RCTs were moderate to high. Seventeen studies were of higher methodological quality and the remaining 2 of moderate quality. The authors were commenting that this fact is appreciable for a relatively new approach with considerable amount of practice variations (Fig 6.1 & 6.2). The literature regarding the effectiveness of MFR was mixed in both quality and results. Though the quality of the RCT studies varied greatly, the results of the studies were encouraging, particularly with the recently published studies. In many RCT's the MFR was adjunctive to other treatments and the potential-specific MFR effect cannot be judged.

From the review, nine studies concluded that MFR may be better than no treatment or sham treatment for various musculoskeletal and painful conditions. Seven studies demonstrated that MFR with a conventional therapy was more effective than a control group receiving no treatment (three studies), sham treatment (one study) or with a conventional therapy. Two other

studies highlighted MFR to be equally effective to conventional or “alternative” treatments (e.g., joint manipulation, back school or hot packs). The review concluded that the MFR can be a useful adjunct to the conventional therapies for various conditions.

## **6.2. Review Process**

The systematic review clearly explains the review process and procedures. The review was performed by selecting RCTs using a detailed electronic database search on MEDLINE, CINAHL, Academic Search Premier, Cochrane library and Physiotherapy Evidence Database (PEDro) by adhering to the systemic review process followed by Mc Kenney et al. (2013) in their study and without any date limitation. Two reviewers performed independent searches, in September 2013 which was later updated in May 2014. Key words used for the search were ‘myofascial release’ and ‘myofascial release therapy’. Each reviewer identified articles as relevant based on the use of the term myofascial release in the abstract or key words. The lists were compared, and articles identified by both reviewers were collected in full text.

## **6.3. Criteria of Selection**

The systematic review was with clear inclusion and exclusion criteria for the selection of the RCTs. (1) RCTs published in a scientific peer-reviewed journal, (2) studies with 10 or more participants, (3) contained sufficient information to complete an analysis, (4) used direct or indirect and passive MFR as an experimental treatment, (5) published in English, (6) studied human participants and (7) adult participants only (18 years and older). The exclusion criteria were (1) published articles as case studies, editorials, expert opinions or instructive articles, (2) used trigger point therapy, (3) not use MFR as defined, (4) Studies on myofascial trigger-point therapy, proprioceptive neuromuscular facilitation (PNF) and MFR used as a conventional treatment without distinct explanations. This can be considered as a comprehensive criterion for isolating and selecting trials studying the therapeutic effectiveness of MFR. The reviewers

collected the number of participants, condition being treated, treatment used, control group, outcome measures and results as the data for analysis.

#### **6.4. Data Analysis Process**

In the systematic review, a total of 133 articles were identified as relevant for a review and 19 were found eligible as per the inclusion criteria. The selected studies were then analysed using PEDro and CEBM Scales for quality and level of evidence. No risk of bias analysis was carried out for this review. A detailed discussion was formatted based on the key characteristics and methodological details of the studies.

#### **6.5. Data Synthesis**

The authors have done an in-depth discussion following the data synthesis in the review. The comprehended summary is added here. “The quality of research on MFR as a treatment varies widely. The recent published studies are appreciable in their adherence to near normal RCT guidelines. The PEDro score for the said RCTs were seven for two studies and six and eight for the remaining two, indicating high quality design. Of the 19 studies included in the systemic review, five RCTs were ranked at levels 1b and 14 at level 2b on the CEBM Scale, indicating relatively high-quality studies. Scores on the PEDro Scale indicated moderate-to-high methodological standards. The lowest score was five out of 10 and the highest was eight out of 10”.

Possible limitations and suggestions for the future trials were given at the end of the discussion and conclusion which is significant for the quality of the analysis.

A brief summary of the RCTs included in the review is given below excluding the 3 RCTs analysed in this thesis earlier. Table 1 briefly explains the studies, their outcomes and scores. Figure 6.1 and 6.2 represents the analysis of PEDro and CEBM score of all the studies included.

## **6.6. Randomised Controlled Trials on Myofascial Release: Others**

### **6.6.1. MFR in the Management of Hamstring Tightness**

Hanten and Chandler (1994) conducted a moderate quality study that was rated at level 2b on the CEBM Scale and 6 of 10 on the PEDro Scale. The purpose of the study was to compare the effect of MFR and PNF in increasing the straight leg raise (SLR) in the management of hamstring tightness. The study highlighted the point that, though MFR is effective in increasing the SLR angle against a control group receiving no treatment, the effect is inferior to a PNF treatment. The study itself had positive outcomes, but it lacked random selection of participants and follow-up.

### **6.6.2. MFR and Pelvic Symmetry**

The study by Barnes (1997) on pelvic symmetry was ranked as level 2b and earned a PEDro score of 8 of 10. Only 10 participants were involved, and the authors acknowledged that 23 participants were needed in the treatment group and 15 in the control group to meet the assumptions for parametric data analysis. Despite these limitations, the 8 of 10 ranking on the PEDro Scale indicated that the study was well designed.

### **6.6.3. MFR for Subacute Low Back Pain**

Hsieh et al. (2002) investigated the relative effectiveness of three manual treatments including MFR for patients with Subacute Low Back Pain (SALBP). The study was rated as a high-quality one, ranked at level 1b on the CEBM Scale and earned 7 of 10 points on the PEDro Scale. The back pain improved in all groups, but there were no differences between the groups. This study concludes that MFR may be used as an adjunct to a formal treatment for SALBP.

#### **6.6.4. MFR for Plantar Fasciitis**

Another level 2b study was performed by Kuhar et al. (2007), who used MFR to treat plantar fasciitis. This study scored 7 of 10 points on the PEDro Scale. Significant reduction in pain and improvement in foot function was reported as the short term effect.

#### **6.6.5. Effects of MFR after High-intensity Exercise**

Arroyo-Morales et al. (2008) in their RCT studied the effects of MFR after high-intensity exercise which scored level 2b in CEBM Scale with a quality of 6/10 on the PEDro Scale. The study included 62 healthy, active individuals. Holter recording and BP measurements were taken after the exercise protocol and after the intervention and found that MFR favours the recovery of heart rate variability and diastolic BP after high-intensity exercise to pre exercise levels. Short duration and lack of follow up along with a normal healthy sample were considered as the limitations of the study since the assumption that high-level sports people might possibly show a different behaviour dropped the study into the 2b level.

#### **6.6.6. MFR and Fascial Mobility**

Tozzi et al. (2011) studied pain perception and the mobility of fascial layers by using a dynamic ultrasound (US) in patients with neck pain (NP) and low back pain (LBP). The groups were evaluated by 'Dynamic US Topographic Anatomy Evaluation', before and after MFR treatment, in the corresponding painful region. The result highlighted that MFR can be effective in releasing areas of impaired sliding fascial mobility and to improve pain perception over a short term duration in people with non-specific NP or LBP. The study obtained 2b level evidence with a quality of 7/10. Main limitations noted were the short term follow up and a relatively small study population.

### **6.6.7. MFR in Temporomandibular Disorders**

A study of 30 chronic myogenous Temporomandibular Disorder (TMD) patients by Kalamir et al. (2010) investigated the effectiveness of intra-oral MFR therapy (IMT) by randomising into three groups; IMT, IMT plus 'self-care' and a wait list control with pain and range of motion (ROM) as the primary outcome measures. They concluded that IMT with or without self-care may be beneficial in chronic TMD over the short and medium term and advocated a larger scale study over a longer term. The study obtained a high quality rating on the PEDro Scale (8/10) and a 2b rating on the CEBM rating.

### **6.6.8. MFR for Gleno-humeral Joint Range of Motion**

Kain et al., in 2011, compared an indirect tri-planar MFR technique and a hot pack for increasing gleno-humeral joint ROM in 31 healthy individuals. Both the hot pack application and the MFR technique were found to be as efficacious in increasing passive ROM of the gleno-humeral articulation. Improper blinding, concealing and follow-up grade the quality of the study as moderate (5/10 on the PEDro) and level 2b on the CEBM.

### **6.6.9. MFR for Fibromyalgia**

Castro-Sanchez et al. conducted two (2011 a, b) high quality studies in fibromyalgia. Both studies were rated as 7/10 on the PEDro Scale and 1b on the CEBM Scale due to their methodological standards. The first one was to determine whether MFR therapy can improve pain, anxiety, quality of sleep, depression and quality of life in patients with fibromyalgia. Right away after treatment and at 1 month, anxiety levels, quality of sleep, pain and quality of life were improved in the experimental group over the placebo group. In the second study 86 fibromyalgia patients were measured to find out the effect of a 20 week MFR on pain, physical function and postural stability over a placebo group. MFR improved pain, sensory and affective dimensions without change in postural stability. They concluded that MFR techniques can be a complementary therapy for fibromyalgia syndrome.



#### **6.6.10. MFR in Breast Cancer Survivors**

Two moderate to high quality studies were found on quality of life of breast cancer survivors (BCS). The first study was by Fernandez-Lao et al. (2012) on the influence of patient attitude towards massage on pressure pain sensitivity and immune system after application of MFR. Twenty BCS, in a two week study, received MFR or control (special attention) intervention. Salivary flow rate, immunoglobulin A concentrations & the attitude toward massage scale were the outcome measures. MFR led to an immediate increase in salivary flow rate in BCS with cancer-related fatigue. Lack of therapist blinding and follow ups were the main drawbacks of the study.

The second study was conducted by Cantarero- Villanueva et al. (2012). Seventy eight BCS participated in a study of the effectiveness of core stability exercises and recovery MFR on fatigue with the 'profile of mood state questionnaire' as the main outcome measure. The experimental group received core stability exercises & MFR while the control group received usual health care advice for a period of 8 weeks. The multimodal program with MFR reduced fatigue, tension, depression, improved vigour and muscle strength. The study was of moderate to high quality (7/10) with level 2b evidence. The main drawback was that the control group was allowed to freely increase physical activity during the study.

#### **6.6.11. MFR for Venous insufficiency in Postmenopausal Women**

A comparative study was performed on the effectiveness of MFR and PT for venous insufficiency in postmenopausal women by Ramos-Gonzalez et al. (2012), which is of high quality (8/10) with a 2b level of evidence. Sixty five postmenopausal women with stage I or II venous insufficiency were enrolled into two groups. The control and experimental group patients underwent physical venous return therapy (kinesiotherapy) for a 10-week period, during which the experimental group patients also received 20 sessions of MFR. The main outcome measures were blood pressure, cell mass, intracellular water, basal metabolism,

venous velocity, skin temperature, pain and quality of life. The combination of MFR and kinesiotherapy improved the venous return, pain and quality of life in postmenopausal women with venous insufficiency. Lacks of follow up and non-blinding of the researchers were the primary limitations.

#### **6.6.12. Lateral Epicondylitis**

Khuman et al. (2013) carried out a study on a smaller sample size of chronic lateral epicondylitis (CLE) subjects. They concluded that a four weeks MFR program was effective in improving pain, functional performance and grip strength in CLE subjects compared to the control group. Lack of follow up and improper blinding were the major limitations. The study scored 2b level of evidence with a quality of 7/10.

#### **6.6. 13. MFR and reaction time**

Kuruma et al., conducted a study (2013) on the effects of MFR and stretching technique on range of motion (ROM) and reaction time (RT) with a medium quality procedure (5/10 in PEDro) and 2b level in CBEM. Passive ROM was significantly increased by MFR in the quadriceps and stretching groups. Premotor time was significantly reduced by MFR in the quadriceps and hamstrings groups. Compared to controls, RT was significantly lower after the interventions in the quadriceps and hamstrings groups. Lack of blinding, concealing and follow up were the main limitations of the study.

#### **6.6.14. MFR and Plantar Heel Pain**

A study by Ajimsha et al. (2014) investigated whether MFR reduces the pain and functional disabilities associated with plantar heel pain (PHP) in comparison with a control group receiving sham ultrasound therapy. Sixty six PHP patients, in a 4 week study, received MFR or control intervention. The study was ranked level 2b on the CEBM Scale and scored 8/10 on the PEDro Scale. The simple main effects analysis showed that the MFR group performed better than the control group in weeks 4 and 12 ( $P < 0.001$ ). A significant ‘pressure

pain threshold' (PPT) changes over the gastrocnemii and soleus muscles and over the calcaneus compared to the control group was reported. The short term follow up was mentioned as the major limitation of the study. The authors recommended future studies to compare the MFR with established treatments like arch supports, self-stretching or even with surgical procedures.

### **6.7. AMSTAR 2 Analysis**

Analysis of the AMSTAR-2 tool (Appendix 10.5) revealed moderate methodological quality of the systematic review. There was 'partial yes' for the protocol as there was no meta-analysis and analysis of heterogeneity done. This was justifiable as the study was purely a systematic review. The comprehensive research strategy also met with 'partial yes' as the study did not attempt to find out the grey literature and articles in press. No details of excluded studies were given the review. The review did not emphasize the study setting or time frame for follow up. The review had positive findings regarding the inclusion criteria, method of selection of eligible studies and the consensus between the reviewers. The major flaw with this review was the noncompliance with the risk of bias analysis. Few details were given regarding lack of blinding but details like sequence generation, allocation and data reporting were not clearly mentioned.

### **6.8. Conclusion**

This systematic review demonstrated moderate methodological quality as per the AMSTAR tool. Omission of a risk of bias analysis was the major limitation of this review. Lack of heterogeneity testing, missing components in the 'comprehensive research strategy' and study setting details were the other limitations found. The authors concluded that the literature regarding the effectiveness of MFR was mixed in both quality and results. Although the quality of the RCT studies varied greatly, the result of the studies were encouraging, particularly with the recently published studies. The review ends by stating that MFR is

emerging as a strategy with a solid evidence base and tremendous potential and the studies in this review may serve as a good foundation for the future trials.

Fig 6.1: PEDro Scale for MFR RCTs (Max value=10)

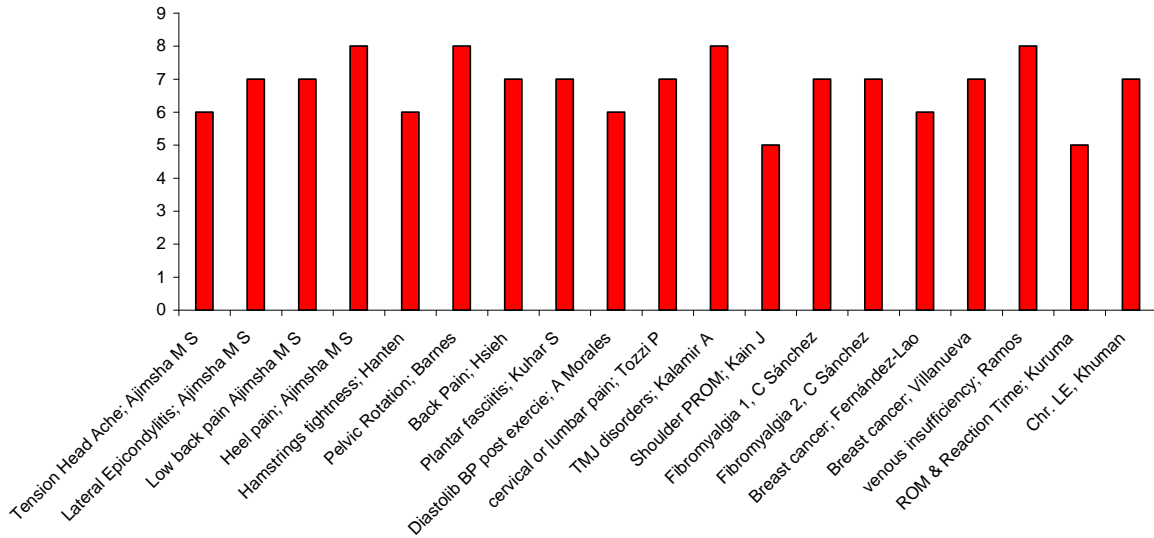
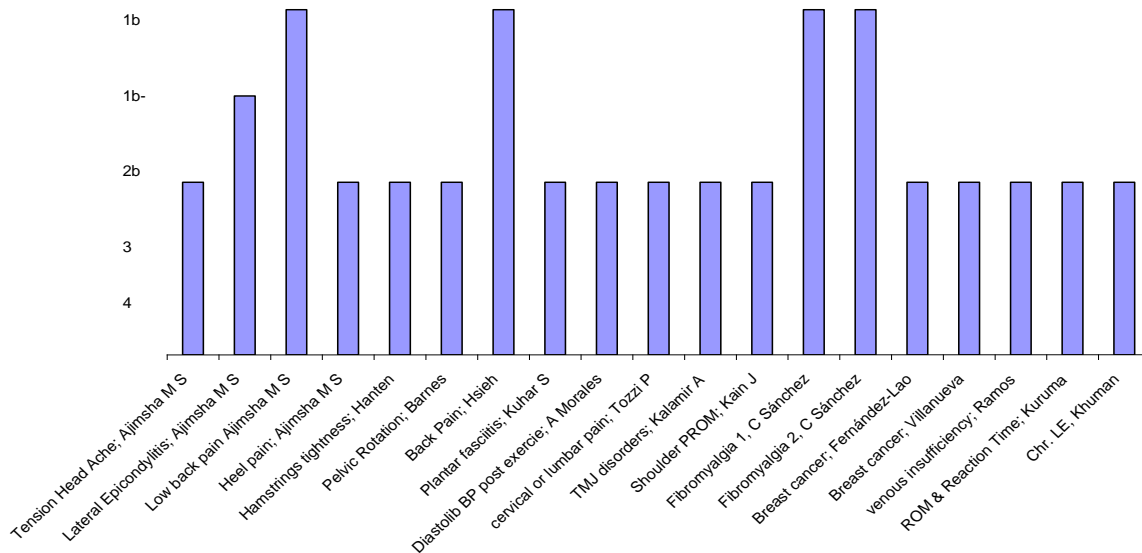


Fig 6.2: CEBM level of evidence score for MFR RCTs



**Table 6.1: Study results & grading included in the systematic review**

First Author Year	Condition	Sample Size	Treatment	Control	Treatment Schedule	Main Outcome Measures	Results	PEDro Score	Level of Evidence (CEBM)
<b>Hanten WP 1994</b>	Hamstrings tightness	75	MFR to leg x 10-15 min, Contract-relax PNF x 4 min	Supine rest x 5 min	Single session	Passive hip flexion ROM	Post treatment gains PNF: 10.4 <sup>o</sup> MFR: 6.6 <sup>o</sup> Control: 0.9 <sup>o</sup>	6/10	2b
<b>Barnes MF 1997</b>	Unilateral Pelvic Rotation	10	MFR pelvic region, 10 min	Rest x 10 min	Single session	Pelvic Position	Better pelvic alignment post MFR	8/10	2b
<b>Hsieh CY 2002</b>	Sub-acute Low Back Pain	200	Back school program, MFR, joint manip or combined MFR + joint manip	NA	Back school :1/week x 3, MFR , joint manip & combined MFR + joint manip: 3/week x 3	VAS, Roland Morris activity scale	Back pain improved in all. No difference between groups	7/10	1b
<b>Kuhar S 2007</b>	Plantar fasciitis	30	Ultrasound x 5 min, contrast bath 20 in, exercises, MFR x 15 min	Ultrasound x 5 min, contrast bath 20 in, exercises	10 consecutive days	FFI, VAS	Significant reduction in VAS and FFI	7/10	2b
<b>Arroyo-Morales 2008</b>	healthy active individuals	62	MFR x 40 min	sham treatment with disconnected ultrasound and magnetotherapy x 40 min	Single session	HRV & BP	favours the recovery of HRV and diastolic BP after high-intensity exercise	6/10	2b
<b>Tozzi P 2010</b>	non-specific cervical(NP) or lumbar pain (LBP)	120	NP: MFRx 6 min LBP: MFR x 12 Min	NP: Sham MFR x 6 Min LBP: Sham MFR x 12 in	Single session	dynamic ultrasound (US)	MFR improved fascial mobility& pain in people with non-specific NP or LBP.	7/10	2b

<b>Kalamir A 2010</b>	chronic myogenous temporomandibular disorders	30	MFR x 15 min, MFR 15 min with self-care & exercises	Waist list	2 sessions/week x 5	ROM & Pain	MFR alone or with self-care is beneficial	8/10	2b
<b>J. Kain 2011</b>	Healthy individual	31	indirect tri-planar MFR x 3 min	hot pack x 20 min	Single session	passive shoulder range of motion	MFR is as effective as hot packs in increasing range of motion	5/10	2b
<b>Castro-Sánchez, AM 2011</b>	Fibromyalgia	74	MFR x 90 min	Disconnected Magnetotherapy x 30 min	1 session/week x 20	VAS, STAI, BDI, PSQI	MFR improved pain & quality of life in patients with fibromyalgia	7/10	1b
<b>Castro-Sánchez, AM 2011</b>	Fibromyalgia	86	MFR x 60 min	sham short-wave and ultrasound treatment x 30 min	2 sessions/week x 20	number of tender points, MPQ and postural stability.	MFR improved pain, sensory, and affective dimensions without change in postural stability	7/10	1b
<b>Ajimsha MS 2011</b>	tension headache	63	Direct MFR x 60 min Indirect MFR x 60 min	Slow soft stroking x 60 min	2 sessions/week x 12	numbers of days with headache	MFR is effective than a control intervention	6/10	2b
<b>Fernández-Lao 2012</b>	Breast cancer	20	Neck and shoulder MFR x 40 min	Special attention & Education x 40 min	2 sessions separated by 2 weeks	Salivary flow rate, immunoglobulin A (IgA) concentrations,	immediate increase in salivary flow rate & IgA	6/10	2b
<b>Cantarero-Villanueva, I 2012</b>	Breast cancer	78	Multimodal exercise and MFR x 90 min	usual care advises	3 sessions/week x 8	POMS	multimodal program with MFR reduced fatigue, tension, depression, & improved vigour & muscle strength	7/10	2b
<b>Ramos-González E 2012</b>	venous insufficiency in postmenopausal women	65	MFR x 50 min x 2 session/week Venous return kinesiotherapy	Venous return kinesiotherapy 2 times daily	10 weeks	blood pressure, venous velocity, skin temperature, pain	Improvement in venous return blood flow, pain and	8/10	2b

			rapy 2 times daily				quality of life noted		
<b>Ajimsha MS 2012</b>	Lateral Epicondylitis (LE) in Computer Professionals	68	MFR x 30 Min	sham ultrasound therapy x 30 min	3 sessions/week x 4	PRTEE	MFR is effective for LE in Computer Professionals	7/10	Ib-
<b>Ajimsha MS 2014</b>	chronic low back pain (CLBP) in nursing professionals	80	specific back exercises (SBE) & MFR x 60 min	SBE & Sham MFR x 60 min	3 sessions/week x 8	MPQ, QBPDS	MFR with SBE is effective for CLBP	7/10	1b
<b>Kuruma H 2013</b>	Healthy individuals	40	MFR to hamstring x 8 Min. MFR to Quadriceps x 8 Min. stretch for quadriceps 8 min,	Lay supine x 8 min	Single session	ROM, muscle stiffness, and Reaction Time	improved ROM & ease of movement	5/10	2b
<b>Khuman PR 2013</b>	Chronic Lateral Epicondylitis	30	MFR forearm x 30 min, Ultrasound x 5 min Stretching and strengthening exercise	Ultrasound x 5 min Stretching and strengthening exercise	3 sessions/week x 4	pain, functional performance & grip strength	significant decrease in pain, improvement in functional performance & grip strength	7/10	2b
<b>Ajimsha MS 2014</b>	plantar heel pain (PHP)	66	MFR x 30 Min	sham ultrasound therapy x 30 min	3 sessions/week x 4	FFI & PPT	significant decrease in pain & functional disability, improvement in pressure pain threshold	8/10	2b

Abbreviations: Myofascial Release (MFR), Not Applicable (NA), Range of Motion (ROM), State-Trait Anxiety Inventory (STAI), Beck Depression Inventory (BDI), Pittsburgh Quality of Sleep Index Questionnaire (PSQI), McGill Pain Questionnaire, (MPQ), Profile of Mood State (POMS) questionnaire, Quebec Back Pain Disability Scale (QBPDS), Chronic Low Back Pain (CLBP), Patient-Rated Tennis Elbow Evaluation (PRTEE). Minutes (Min), Manipulation (Manip), Centre for Evidence-Based Medicine (CEBM), Proprioceptive Neuromuscular Facilitation (PNF), Visual Analogue Scale (VAS), Foot Function Index (FFI), Heart rate variability (HRV), Blood Pressure (BP), Foot function index (FFI), Pressure pain threshold (PPT).

## **Chapter 7**

### **Discussion**

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*7.1. Discussion*

*7.2. The Randomised Controlled Trials*

*7.3. The Systematic Review*



# Chapter 7

## Discussion

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### 7.1. Introduction

Recent studies have demonstrated the role of fascia in various musculoskeletal dysfunctions as the fascial tissues connect the skeletal muscles forming a body-wide web with some pattern called as myofascial meridians. As fascia is able to modify its tensional state, strain transmission along the meridians might occur in response to changes of muscle activity. (Wilke et al., 2016).

Fascia is a ubiquitous tissue permeating the entire body. It surrounds, supports, suspends, protects, connects and divides muscular, skeletal and visceral components of the organism (Kumka and Bonar, 2012). It not only lubricates the fibres but gives nourishment to all parts of the body. The fascial system is considered as a “tensegrity” or tensional integrity structure to manage the balance between tension and compression around the organs, joints and muscles (Chen et al., 2016). Its continuity aids in force transmission both longitudinally and epimuscularly through mechanotransduction. These forces may be transmitted at a cellular level, altering gene expression of fibroblasts and thereby changing the extracellular matrix composition (Chaitow, 2016). Repetitive mechanical straining of fibroblasts can also result in secretion of inflammatory mediators (Dodd et al., 2006). All of these changes could affect the normal functions of force transmission or sliding in the musculoskeletal system. This dysfunction could lead to pain or proprioceptive issues, considering that fascia has been shown

to be innervated. Thus, treatment of disorders affecting the musculoskeletal system may need to be focused on this fascial network (Kwong and Findley, 2014).

The fascia plays different physiological and functional roles related to joint stability, general movement coordination, proprioception and nociception and is associated with wound healing, tissue repair and many connective tissue pathologies. The myofascia, as a fibrous specialization of fascial/ECM tissues that surround and interpenetrate muscles is then a complex hierarchy of helically-reinforced tubes contained within larger tubes that surround the muscles, the limbs and entire body. The cross helical model of fascial fibre arrangement are indeed contributing to the coordination of changes in muscle shape. It appears that the fascia mediates an active mechanical transference role as it provides dynamic connections between and among the muscles and bones (Yang et al., 2015). Functional myofascial sequences are directly involved in the organization of movement and muscular force transmission (Kwong and Findley, 2014)

Studying fascia objectively at the basic science and clinical levels will provide important information that may change clinical practice. Once the structure and functions of fascia in the musculoskeletal system are further elucidated, the pathophysiology of many disorders and their consequences may be better explained.

Myofascial release (MFR) is a form of manual therapy which involves the application of a low load and long duration stretch to the myofascial complex intended to restore optimal length, decrease pain, and improve function (Barnes, 1990). The rationale for these techniques can be traced to various studies that investigated plastic, viscoelastic and piezoelectric properties of connective tissue (Schleip, 2003; Greenman, 2003; Pischinger, 1991). MFR is being used to treat patients with a wide variety of conditions, but there is scarcity of evidence to support its efficacy.

The effects of manual fascial interventions can be local (as tissue texture changes), segmental (as via neurological response) and global (as through hormonal effects) in extent, and may occur at different intervals—ranging from minutes to weeks—after a given input, with many interacting mechanisms influencing tissue properties and behaviours, including placebo. Some of these factors are strongly supported by the available evidence whereas others need further investigation (Tozzi, 2015b).

Various forms of manual loading, whether sustained or cyclical, that differ in direction, speed, magnitude and frequency, appear to exert a strong impact on cell behaviour, gene expression and tissue remodelling through growth factors and enzyme activation (Tozzi, 2015a). MFR brings sustained change in the architecture and/or hydration of the fascia being worked on. The mechanical loading of fascia causes changes through activation of fibroblast response and the different receptors present in the fascial tissue, leading to modulation of myofascial contraction (Hicks et al., 2014). The fascial tissue may respond better to balanced and sustained stretch rather than intermittent and unequal loads (Meltzer et al., 2010).

Brief, light/moderate, balanced, static or slow cyclic strains appropriately applied to fascia may be sensed at the cellular level and transduced in normalizing tissue structure and function (Tozzi 2015b). Fascial oriented work may produce beneficial effects by activating various receptors in the connective tissues that elicit a series of neuromuscular reflexes. These types of events occur together with concomitant autonomic and viscoelastic changes and are more likely to explain the fast tissue responses that a therapist perceives during fascial techniques. Fascial therapy theoretically restores mobility by re-optimizing the distribution of lines of force within fascia (Stecco et al., 2013; Day et al., 2009). Encouraging explanations and evidence are accumulating day by day regarding the effectiveness of MFR and an attempt to merge the clinical effectiveness with physiological alterations of fascial manipulation will improve the understanding of the fascial functions and its significance in health and wellbeing.

Studies are emerging in this field with varying results and conclusions. Analysis of the recent research trials and reviews will be a better way to appraise the quality and reliability of such work. This work attempts to critically analyse three published randomised controlled trials (RCTs) and one systematic review on the effectiveness of myofascial release on various conditions with an aim of facilitating the creation of a more homogenous and reputable base for future trials in the field. A critical appraisal of the conducted studies and reviews to pinpoint their strengths and weaknesses can help to fine tune future studies. This type of approach and its findings can be highly useful for a manual therapy technique having lots of practice variations and applicability to set more controlled and methodologically superior studies in the future.

## **7.2. The Randomised Controlled Trials**

Three RCTs on MFR were analysed in this review. The three published RCTs were appreciable in their adherence to near normal RCT guidelines. Among the RCTs reviewed, one study was ranked at level I b in CEBM and 7/10 in PEDro Scale, the second one ranked as I b- in CEBM and 7/10 in PEDro rating. The third one was ranked as 2b level in the CEBM Scale with a PEDro rating 6/10.

The effectiveness of MFR on tension type headache (TTH) was the first among the studies reviewed as this was the first published study (2011) in the list. TTH is a bilateral headache of a pressing or tightening quality without a known medical cause. MFR is currently being applied for patients with TTH but its efficacy was not been evaluated formally. Sixty three patients with episodic or chronic tension-type headache were given direct MFR technique, indirect MFR and a sham treatment and were compared. The study was of moderate quality (6/10) on PEDro with 2b level of evidence in CEBM Scale. The techniques were applied for 24 sessions per patient over 12 weeks with the difference in number of days with headache at baseline and post-test as the outcome measure. Patients in the direct MFR group, the indirect

MFR group and the control group reported a 59.2%, 54% and 13.3% reduction respectively in their headache frequency in post-test compared to the baseline with decreases of the number of days with headache per four weeks by 7.1 (2.6) [mean (SD)] days in the direct MFR group compared with 6.7 (1.8) days in the indirect MFR group and 1.6 (0.5) days in the control group ( $P < 0.001$ ). Both the direct and indirect techniques of MFR investigated in this trial were more effective than a control intervention consisting of slow soft stroking with finger pads for the treatment of TTH. The authors were optimistic that a significant proportion of patients with TTH might benefit from the use of MFR. This study proved that direct technique or indirect technique MFR was more effective than a control intervention for TTH. Lack of follow up, blinding of the therapists and the patient were the major limitations of the study. A risk of bias analysis identified the blinding of patients and sample calculation as the major draw backs. There was no attempt made to explain or discuss the mechanisms underlying these responses as the principle objective of the study was to find the clinical efficacy.

The second RCT studied MFR as a treatment for lateral epicondylitis (LE) which was completed with 68 patients. The study investigated whether MFR reduces pain and functional disability of LE in comparison with a control group receiving sham ultrasound therapy (SUST) in computer professionals for 12 sessions per client over four weeks with the Patient-Rated Tennis Elbow Evaluation (PRTEE) as the main outcome measure taken after the treatment (four weeks) and in follow up (12 weeks). The study was of a moderately high quality on the PEDro Scale (7/10) with 1b- level in CBEM. The study found that the MFR group performed better than the control group at weeks 4 and 12. Patients in the MFR and control groups reported a 78.7% and 6.8% reduction, respectively, in their pain and functional disability in week four compared with that in week one, which persisted as 63.1% in the follow-up at week 12 in the MFR group. Lack of therapist blinding was the major limitation of the study. A slight improvement over time occurred in the control group at week four and the authors were

attributing this to a 'meaning response'. The results of the study suggest MFR as a beneficial tool for managing LE in computer professionals. This study was limited by a short follow up period and very few and self-rating outcome measurements. Future studies with sufficiently powered sample sizes and longer follow up periods should be completed to verify these results.

The third RCT was on chronic low back pain. Eighty nursing professionals (aged 20 to 40 years) with chronic low back pain (CLBP) (pain for 3 or more months) were randomly assigned into 1 of 2 groups to determine if MFR effectively reduces CLBP. The study was a high quality one (PEDro score of 7/10 and CBEM level of 1b). The aim was to investigate whether MFR when used as an adjunct to specific back exercises (SBE) reduces pain and disability in CLBP in comparison with a control group receiving a sham MFR and SBE among nursing professionals. The McGill Pain Questionnaire (MPQ) was employed to assess subjective pain experience and Quebec Back Pain Disability Scale (QBPDS) was employed to evaluate the disability associated with CLBP. The primary outcome measure was the difference in MPQ and QBPDS scores between week one (pre-test score), week 8 (post-test score), and follow-up at week 12 after randomization. The patients in the MFR group reported a 53.3% diminution in their pain and 29.7% decrease in functional disability as evidenced in the MPQ and QBPDS scores in week 8, whereas patients in the control group reported a 26.1% and 9.8% decrease in their MPQ and QBPDS scores in week 8, which persisted as a 43.6% reduction of pain and 22.7% reduction of functional impairment in the follow-up at week 12 in the MFR group compared to the baseline. The proportion of participants responded to treatment (i.e. at least a 50% reduction in pain from week 1 to 8) was 73% in the MFR group and 0% in the control. No patient within the MFR or control groups exhibited a 50% reduction in functional disability within the first 8 weeks. The authors advocated examining other outcomes such as pain beliefs, mood, and quality of life in future studies. The major limitations quoted were lack of blinding of the practitioners, lack of long term outcomes and over dependence on self-rating

scales as explained in the previous RCTs. This study provides evidence that MFR when used as an adjunct to SBE was more effective than a control intervention for CLBP in nursing professionals. A significant proportion of nursing professionals with CLBP might benefit from the use of MFR. The mechanisms underlying these responses merit further investigation.

### **7.1.1. Strength and Weakness**

Even though the RCTs analysed were methodologically superior with higher quality compared to many studies in this field, there were many limitations to be pointed out. The primary research aim to undertake the MFR RCT trials was to create a respectable base for the future trials in this field. An attempt to convert the ‘practice based evidence’ to evidence based practice starting from the anecdotal evidences was challenging in many ways. The involved studies were published during the period 2011-2014 in reputed journals of health and rehabilitation.

The main limitations of all the RCTs were that the samples were underpowered as none of the studies have attempted a sample size calculation. It is to be noted that most of RCT trials were ‘proof of concept trials’ in those conditions. No previous evidence was available other than anecdotal evidence for most of the studies and most of the conditions under the clinical picture of Myofascial pain syndrome does not have any clear prevalence to go for any sort of power calculation and was the main concern of many of the researchers in this field. With the sufficient number of emerging good quality RCTs and systematic reviews, we believe that the sample size calculation sufficient enough to achieve external validity will be comparatively achievable for the forthcoming studies.

The allocation sequence was adequately generated for all the three RCTs by utilizing a computer generated randomization list by blinded statisticians who were not a part of the study and without any information of the treatment procedures. The allocation was adequately concealed too. The RCT on the effectiveness of MFR on TTH was affected with a performance

bias as the patients were aware of the treatment that they are going to get. This was the first study in the MFR–RCT series and few patients accidentally exchanged the information on the waiting area on the initial days, the authors reported that, this was managed by giving specific date and time for each patient for their sessions. Such incidents and biases were not reported in the later trials.

The blinding of the assessors was mentioned in all the RCTs, with two assessors having no knowledge of the study process or randomisation for all the three studies. Blinding of the therapists was an issue in all the RCTs. Blinding of the therapist and the patients in manual therapy is a much-debated topic in the physical therapy research and it is mainly due to the type of approach the physical therapy field generally has. The missing of outcome data was mentioned in all the RCTs. In the study of MFR in TTH, it was mentioned, 2 participants from the DT-MFR group and one participant each from the remaining two groups dropped out of the study without providing any specific reason for this. The authors of the study found that the total number of recruited individuals was 60 but was mentioned as 63 in the printed version. In the study published in 2012, the MFR in LE, 65 participants out of 68 completed the study protocol. One from the MFR group and two from the control group dropped out during the study. In the third RCT on CLBP, two participants from the MFR group 4 from the control group dropped out of the study without providing any specific reason and this data were excluded from the results. The main reason for this drop out was reported as due to the inability to attend the sessions on the scheduled day and time as a minimum one day gap was advised between the treatments in the protocol.

All the three RCTs and most of the RCTs reviewed in the systematic review were relying primarily on patient rated outcomes measures (PROMs). Whilst this reflects the contemporary model of technical rationalism in manual therapy practice (Thomson et al., 2014) to provide a more balanced view, more objective and sensitive outcome measures which can



measure more clinically beneficial outcomes are advocated. This is in fact, a highly debated topic in current clinical research. According to Kyte et al. (2015), the use of PROMs is set to rise in physiotherapy as high-quality clinical care requires patients to provide information regarding how they are feeling, their symptoms and any effects of prescribed treatment. The medical outcomes study was at the forefront of this concept as patient outcomes were examined and differences in care, clinicians and communication styles were reported for both patient and clinical outcomes (Tarlov et al., 1989). The separation between health outcomes and treatment outcomes became clearer when research into health services began to focus on improving the patients' health-related quality of life, particularly when patients were undergoing optimal medical therapy (Wilke et al., 2004). This, in turn, created the need for identifiable, valid and reliable PROMs. Traditional survival, disease, and physiological outcomes may demonstrate the physiological benefits of treatment; however, the patient perspective provides a more holistic interpretation and a comprehensive assessment of the benefits of the treatment under investigation (Black, 2013; Rathert et al., 2011). PROMs provide additional 'patient-centred' data which are unique in capturing the patient's own opinion on the impact of their disease or disorder and its treatment on their life. Thus, PROMs are increasingly used by clinicians to guide routine patient care or for the purposes of audit and are already firmly embedded in clinical research (Kyte et al., 2015). This review supports the view of Weldring and Smith (2013) that when clinical trials involve conditions in which there is no objective outcome measurement, such as the degree of morbidity or biomarkers for symptoms, and in which outcomes can only be observed subjectively to the patient in terms of impact; PROMs can be used as primary outcome measures. We believe that disease specific PROMs are more idealistic as primary outcome measures as they have greater face validity and credibility than generic PROMs, but these comparisons cannot always be made across a variety of conditions. The inclusion of PROMs with clinical outcomes in research and clinical practice can provide a more

complete understanding of the impact of an intervention, therapy, and/or service on the patient (Weldring & Smith, 2013).

The outcome measures used in the studies, difference in headache days from headache diaries in TTH trial, Patient Rated Tennis Elbow Evaluation (PRTEE) Scale for LE trial, McGill Pain Questionnaire (MPQ) and Quebec Back Pain Disability Scale (QBPDS) in CLBP were the commonly used scales in this area of research with acceptable reliability, validity and sensitivity. Reliance on PROMs often makes the outcome validity questionable especially with recall bias. The three trials included have reported that the outcome objective and patient improvement were assessed in a manner to limit bias even though the details were not present. Factors such as quality of life, patient perceptions of change and impact on patients' believe and moods could have been also included in these trials.

Details about the expertise/experience of the practitioners were mentioned in all RCTs, as MFR trained with a median MFR experience of 12 months or more. All the studies were emphasizing the implementation of protocol based treatments. Protocols were mentioned for all the patients in the MFR or control groups. It was pointed that after the base line assessment by the blinded assessor, the participants were handed over to a therapist with a protocol that he has to follow as per the said frequency, duration and timing and need to report any adverse events through the adverse event reporting system.

All the studies plotted the blinding of the practitioner as the main problem that they encountered. Another major limitation identified was the inability of long-term follow up of study participants. Few of the earlier pilot studies with long term follow up failed to get sufficient data to have a statistical analysis attributable to the geographical area of the study where people stay mainly for education and jobs. So it was difficult to understand whether the differences observed at post-treatment were maintained over a longer time period. In the LBP trial, the author was mentioning their inability to include other outcome measures such as pain

beliefs, mood and quality of life as one of their limitations. Although there have been many scientific advances in the understanding of the neurophysiology of pain, precisely assessing and diagnosing a patient's chronic pain problem is not straightforward or well-defined. How chronic pain is conceptualized, its influences, how it is evaluated are the factors considered when a chronic pain diagnosis is made. There is no one-to-one relationship between the amount or type of organic pathology and pain intensity, but instead, the chronic pain experience is shaped by a myriad of biomedical, psychosocial (e.g. patients' beliefs, expectations, and mood) and behavioural factors (e.g. context, responses by significant others). Assessing each of these three domains through a comprehensive evaluation of the person with chronic pain is essential for treatment decisions and to facilitate optimal outcomes (Dansie & Turk, 2013).

The other major issue with the result interpretation was the effect in the control group. The authors believed that the therapeutic touch, feeling of care and treatment have an effect on the participant, and they were attributing this as due to “meaning response” (Moerman & Jonas 2002). None of the studies attempted an effect size calculation. Reporting effect sizes or estimates is considered good practice when presenting empirical research findings in many fields. It is recommendable for the future studies to have effect size or estimate of effect [EE] as part of their statistical analysis.

The authors maintained a common theme for most of the introduction and discussion part as according to them, the aim was to prove the MFR effectiveness on different conditions than conducting studies for analysing different variables. As the need and significance of this analysis mentioned, the main idea of the conducted researches were to create respectable base for the future trial in this field. Since MFR practices vary from clinician to clinician or studies to studies, the authors mentioned that there emphasize was on the ‘uniformity of the practice’.

### **7.3. The Systematic Review**

A systematic review was an exhaustive review of the literature addressing a clearly defined question, which uses a systematic and explicit methodology to identify, select and critically evaluate all the relevant studies and collect and analyse the data emerging from the studies included in it. Systematic reviews establish whether the scientific findings of research studies are consistent and whether these findings can be generalised to different populations, limiting the various possible forms of bias and increasing the reliability and precision of the estimates.

The systematic review on MFR which was published in 2015 assessed the quality, results and limitations of 19 RCTs found in a multi-database literature search of peer-reviewed articles in the English language. Analysis was completed using the Physiotherapy Evidence Database (PEDro) scale and the Centre for Evidence-Based Medicine's (CEBM) Levels of Evidence scale. Of the 133 studies identified, 19 RCTs were eligible as per the inclusion criteria. The selected RCTs assessed a total of 1228 patients with the sample sizes varying from 10 to 200 with a mean (SD) of 65 (44) patients. Of 19 RCTs, 17 were of high methodologic quality and 2 with moderate methodologic quality, with the lowest score of 5/10 and the highest of 8/10 in PEDro Scale. CEBM Scale categorised 14 RCTs in the 2b level of evidence (ie, small sample size and no long-term follow-up) and the other 5 as 1b. In many of these trials, the MFR treatment was adjunctive to other treatments and the potential specific MFR effect could not be determined. MFR was demonstrated to be equal to or more effective than sham, conventional, and no treatment for various musculoskeletal and painful conditions. The recent RCTs were methodologically superior with higher quality compared to the former ones.

Nine studies concluded that MFR may be better than no treatment or sham treatment for various musculoskeletal and painful conditions. Seven studies demonstrated that MFR with a conventional therapy was more effective than a control group receiving no treatment (three

studies), sham treatment (one study) or with a conventional therapy. Two other studies highlighted MFR to be equally effective to conventional or “alternative” treatments (e.g., joint manipulation, back school or hot packs). These data suggest that the MFR can be a useful adjunct to the conventional therapies for various conditions.

The authors quoted that “MFR may be useful as either a unique therapy or as an adjunct therapy to other established therapies for a variety of conditions like subacute low back pain, fibromyalgia, lateral epicondylitis, plantar fasciitis, headache, fatigue in breast cancer, pelvic rotation, hamstring tightness etc.” The reviewers concluded that MFR is emerging as a treatment strategy with a solid evidence base and that the studies in this review may help as a respectable base for future trials. In assessing the validity of this systematic review, it had clear inclusion and exclusion criteria and a sensitive search strategy. Included trials were assessed for quality using recognized critical appraisal tools. Overall, this systematic review is recommendable as a starting point for assessing the quality and variety of available evidence on the efficacy of MFR.

Analysis of the systematic review with AMSTAR-2 tool revealed a moderate methodological quality. The review had positive findings regarding the inclusion criteria, method of selection of eligible studies and the consensus between the reviewers. The major flaw with this review was the noncompliance with the risk of bias analysis. The comprehensive research strategy met with a ‘partial yes’ as the study didn’t attempt to find out the grey literature and articles in press. No details of excluded studies were given in the review.

### **7.3.1. Evaluation of the Validity of the Review**

Even though the systematic review clearly focused on MFR, the included studies were very heterogeneous in terms of population included, type of MFR administered, control groups, outcome measures, timing of follow-up and presentation of data. This might have affected the validity of the result and its generalization. Since MFR can be useful on a variety of condition

and relies on therapist patient interaction, the inclusion criteria might not be sufficient enough to streamline the result of the review. Although attempts were made to find all published RCTs, some relevant trials might have been overlooked including the language constraints. The identified studies have been evaluated for methodological quality by the PEDro Scale and the CEBM Scale and a risk of bias analysis was not done for the review. This might have an impact on the results interpreted, considering the varying quality and standard of the RCTs reviewed. An analysis of the possible biases or flaws might be an ideal component for the limitation part. The methodological quality evaluation was carried out by two independent reviewers and no details were given regarding the degree of agreement between them. This systematic review might be affected with reporting bias as four out of 19 RCTs included were from the principle author, but this was managed by selecting two independent evaluators not having any direct knowledge or expertise in MFR, once the author blinded the identified studies. The name of the authors, the journals, the country of origin and the results were concealed from the independent reviewers, as this information could theoretically influence the evaluation.

As the systematic review of RCTs on MFR satisfies many of the factors necessary for internal validity, it can be assumed that the results emerging from the review will reflect the true effect of the intervention and it is less likely that they could have been influenced by other factors in a level which can influence the result. Restricting searches to databases of peer reviewed literature was another potential limitation including the so-called 'grey literature' would reduce potential publication bias, but would have likely increased data heterogeneity. Nonetheless, despite their heterogeneity and potential statistical conclusion validity issues, from the overall results, it can be inferred that it is worth running large scale trials to explore the effect of MFR in managing various conditions

### **7.3.2. Interpretation of the Results of the Review**

It is not uncommon that individual studies from a systematic review show different and even contradictory results. It is also relatively common to find that although the results of individual studies agree on the efficacy of a therapy, they do not agree on the magnitude of its effect. The reviewer tried to mention such issues like the heterogeneity of the population, treatments applied, outcome measure usage and assessment and the quality of studies included. The populations included in the studies could differ with regard to certain characteristics which influence the outcome such as the severity of the disease and population characteristics including but not limited to age, sex, health status etc. The reviewers commented on the heterogeneity in the treatments administered, and they were justifying it as a common problem faced by every manual therapy intervention. It is a much-recognized limitation of manual therapy as there is huge variation in the practice including, but not limited to, the pressure, technique, treatment times and engagement. It is appreciable that the authors were reporting these issues in their discussion part. They concluded this session with the comment that “until evidence is available on the possible mechanism of action of MFR, or until different interventions have been compared directly, there is no logical basis for choosing the optimal intervention” which is true in any type of manual therapy including MFR. The systematic review also revealed the reporting of the experience of the therapist in MFR as that, few studies only mentioned it, thus pointing towards a procedural bias. The session concludes by lauding on the reporting of adverse events as “different studies might have used different definitions of adverse reaction, research designs or styles of MFR in their studies”.

Since the diversity of the cases included in the review was huge, the outcomes measured in the RCTs were also different with regard to the technique, the frequency or the criteria used which could jeopardize the comparability of results between studies. There is no doubt that the scientific methodological quality in which a study is conducted could modify its results and

the differences between studies could be attributed to the differing qualities of the methods. The review did not carry out any homogeneity test. It was possible to evaluate the probability that the differences between the results were exclusively due to chance and not to the factors mentioned above. Nevertheless, a clinical view of the differences may be more informative than the result of a hypothesis test as the differences may have no statistical significance but actually be of clinical importance and vice versa. It was to be mentioned at this point the heterogeneity of the studies included was mainly due to the vast range of applicability of MFR and the methodological quality rated by the scale did not plot any unusual findings of the included RCTs. This might be the reason for the review team not incorporating any homogeneity or sensitivity tests to detect such issues and moreover the review in any steps did not attempt a meta-analysis.

The two scales used for methodological quality of the included RCT were known for their ability to measure methodological quality and clinical hierarchy. A possible risk of bias analysis, if present, was an added advantage. The authors of the systematic review explain clearly that there was an issue with the protocol used in the studies reviewed as some studies used a fixed protocol while a few of them used a flexible one. It is acceptable that in manual therapy both methods are acceptable and have to be considered as valid until the research has advanced towards dose-response levels. The team reported varying levels of effectiveness and concluded that MFR effectiveness appears to be ‘encouraging’ and has ‘tremendous potential’, especially within ‘recently published studies’.

Most of the studies reviewed did not have clear details about the blinding and most of the RCTs reported the blinding of the therapist and the patient as limitations. This can be justifiable considering the special characters that the manual therapy generally and MFR specifically exhibit in the interaction and application part. According to Franke et al. (2014) therapist or patient blinding within manual therapy trials are impossible. There were also larger



issues surrounding generalizability of strictly-controlled RCT-derived results into general manual therapy practice as required by an evidence-based model (Milanese, 2011). There is evidence that MFR alone or added to other conventional therapies relieves pain and improves function not less than conventional therapies studied. According to these results, MFR may be useful as either a unique therapy or as an adjunct therapy to other established therapies for a variety of conditions as mentioned in the review. The review also highlights the fact that ‘the magnitude of the effects were mostly retained’ in studies with follow ups even though such studies were less in number.

Though the result of the review was pointing towards advocating its usefulness, there were a number of threats that challenge the statistical inferences underpinning these findings. Due to the high levels of data heterogeneity and underpowered sample size within trials, generalization of results was almost impossible. Results could not be concluded into a definitive statement on the effectiveness of MFR. The authors of the review in the beginning part of the discussion initiates this point with the statement, “it seems reasonable that in the authors’ qualitative synthesis, the best evidence would be provided by the higher quality studies which are less likely to have biased results”. This review supports the norm that it is unlikely that usage of any other rating system would have given a different result.

The authors were pointing towards the higher possibility of the type I error this review can produce due to the underpowered samples tested and recommending caution on the result interpretation. All reviewed RCTs set a priori significance levels of  $p \leq 0.05$ , a level known to generate false positive findings in at least 30% of adequately powered studies and much higher percentages of false positive findings in underpowered studies (Colquhoun, 2014). The authors were indirectly mentioning the chance of super-realisation bias in the studies as most of the studies were with a relatively smaller sample size which in turn will produce more tightly controlled delivery of interventions and the collection of outcome data in ways that are not

logistically possible in larger ones (Crocker et al., 2013). This is not to say that the small trial results are therefore intrinsically biased, but pooling data from a number of these relatively well-controlled small trials may create a positive bias; pooling data from a series of small trials is not a substitute for a large scale trial (Slavin & Smith, 2009).

### **7.3.3. Applicability of the Results of the Review for Clinical Practice**

It is impossible to actively promote implementation of the results of all systematic reviews because of the limited capacity of health systems to absorb the new evidence and implement the necessary measures to do away with the obstacles that hamper translation of the results of theory into practice. With underpowered sample size and the heterogeneity of the studies, we cannot argue that MFR need to be there in the management of the conditions studied in this review. This review can only suggest to clinicians that there is evidence that MFR alone or added to other conventional therapies, relieves pain and improves function not less than conventional therapies. To have more powerful recommendations, we need studies with properly calculated sample sizes, adequate power, more reliable and validated outcome measures, follow-up time points and appropriate levels of significance.

If a therapist is looking at the results of a study he/she must consider the feasibility of selecting and applying a particular MFR technique based on the environment, the options available, the usage of best practices, the expertise of the staff in MFR, type and stage of the condition as well as factors such as the training of staff. If required, changes in established practice in the service and the acceptance by patients or their relatives that this new intervention should be applied to them. The patient and the therapist should both feel at ease around one another. The experience and training of the myofascial therapists who gave the treatments were mentioned in a few studies mentioned in the review. In other way one can say that MFR can be a non-invasive, non-pharmacological and low cost alternative for various conditions with very minimal adverse events.

Recommendations for future randomised, effectiveness trials on MFRs include: a-priori calculated sample sizes, adequate power, reliable and validated outcome measures, limiting the sources of bias, follow-up time points beyond 24 hours and appropriate levels of significance, assessing the threats to statistical validity and appropriate registration. Most importantly, RCTs should present between group differences (complete with confidence intervals and effect sizes) and desist from reporting within group differences as evidence of effectiveness (Matthews and Altman, 1996; Schulz et al., 2010).

Sample size calculation is one of the first and most essential parts of designing a good quality trial. To make a definitive conclusion about the findings of an RCT, it is essential to ensure at least 80% power throughout the trial. For ethical and methodological purposes, we strongly recommend involving an epidemiologist or a biostatistician at the planning stage of a study, because these calculations are prone to bias and because there are ethical and financial costs related to conducting an RCT. A well-planned and methodologically sound protocol will have a strong chance of success.

These recommendations would support inferences of clinically meaningful results and facilitate future meta-analyses. We echo current calls for transparency within all clinical trials and endorse journal adoption of reporting guidelines (Hoffmann et al,2014; Chan et al., 2014).

Finally, it is admirable to the conclusion of the authors, “to attain the highest-quality evidence, RCT designs should be good quality, participants should be randomised, adherence to the double blinding and the clinician performing the MFR should use it regularly in clinical practice”. They have added that the subjective component of MFR must be addressed in future study designs as it is having a major relevance in this type of studies. It is very clear that the effectiveness of MFR can vary with the comfort level of the patient controlling of which is difficult but not impossible.

In conclusion, this systematic review demonstrated moderate methodological quality as per the AMSTAR tool. Omission of a risk of bias analysis was the major limitation of this review. Lack of heterogeneity testing, missing components in ‘comprehensive research strategy’ and study setting details were the other limitations found. The authors concluded that the literature regarding the effectiveness of MFR was mixed in both quality and results. Although the quality of the RCT studies varied greatly, the result of the studies were encouraging, particularly with the recently published studies. The review ends by coining that MFR is emerging as a strategy with a solid evidence base and tremendous potential and the studies in this review may serve as a good foundation for the future trials

It was appraisable that the systematic review ends with suggestions of refinement to be incorporated in the future trials like studying of clearly defined medical conditions, controlling the intrinsic and extrinsic factors to the maximum possible level, studying the effectiveness of MFR as single therapy and comparing it with a control (no-treatment) group and with other established treatments. The authors were hopeful that by adhering to such guidelines in the future will surely result in much higher quality studies producing more accurate results. This analysis supports many of the norms put forward by the systematic review team and believes that such attempts will make the research in physical therapy field more valid and reliable.

Critical appraisal is an important element of evidence-based medicine to carefully and systematically examine research to judge its trustworthiness, its value and relevance in a particular context. This analysis concludes with a statement that ‘the three RCTs and systematic review analysed in this thesis have the potential to move the Myofascial release research into the next level, though methodological flaws and interpretation biases were evident’. These attempts should be highly appreciated as this will create reputable backgrounds on which the future trials can be built on.

## **Chapter 8**

### **Conclusion**

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#### ***8.1. Conclusion***

## Chapter 8

### Conclusion

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#### 8.1. Conclusion

Fascia is a ubiquitous tissue permeating the entire body. It surrounds, supports, suspends, protects, connects and divides muscular, skeletal and visceral components of the organism. The fascial system is considered as a ‘tensegrity’ or tensional integrity structure to manage the balance between tension and compression around the organs, joints and muscles. Studying fascia objectively at the basic science and clinical level will provide important information that may change clinical practice. Once the structure and functions of fascia in the musculoskeletal system are further elucidated, the pathophysiology of many disorders and their consequences may be better explained.

Myofascial release (MFR) is a form of manual therapy which involves the application of a low load and long duration stretch to the myofascial complex which is intended to restore optimal length, decrease pain and improve function. The rationale for these techniques can be traced to various studies that investigated plastic, viscoelastic, and piezoelectric properties of connective tissue. MFR is being used to treat patients with a wide variety of conditions, but there is scarcity of evidence to support its efficacy. The effects of manual fascial interventions can be local, segmental and global in extent and may occur at different intervals—ranging from minutes to weeks—after a given input with many interacting mechanisms influencing tissue

properties and behaviours including placebo. Some of these factors are strongly supported by the available evidence whereas others need further investigation.

This work attempted to critically analyse three published randomised controlled trials (RCTs) and one systematic review of myofascial release with an aim of facilitating the creation of a more homogenous and reputable base for the future trials in the field.

Three randomised controlled studies on MFR were analysed in this review. The RCTs analysed in this study were of moderate to high methodological quality (PEDro Scale), with higher level of evidence (CEBM Scale) and fewer bias (RoB). The effectiveness of MFR on tension type headache was the first among the studies with a moderate methodological quality (6/10 in PEDro) and with 2b level of evidence in CEBM Scale. The study proved that direct technique or indirect technique MFR was more effective than the control intervention for tension headache. The second RCT studied MFR as a treatment for lateral epicondylitis. The study was of a moderately high quality on the PEDro Scale (7/10) with 1b- level in CEBM. This study verified that MFR was more effective than a control intervention for LE in computer professionals. The RCT on chronic low back pain also scored 7/10 in the PEDro Scale and 1b in the CEBM Scale. This study confirmed that MFR can be a useful adjunct to specific back exercises than a control intervention for CLBP.

Even though the RCTs analysed were methodologically superior with higher quality compared to many studies in this field, all the three RCTs stated the usage of self-report measures and underpowered sample size as the major limitations along with a performance bias reported in the TTH trial. Limitations including improper blinding of the therapists and the patients, recall and reporting bias, long term follow up issues and lack of effect size calculation were a few among them. The missing of outcome data was mentioned in all the RCTs. The three trials included have reported that the outcome objective and patient improvement were assessed in a manner to limit bias even though the details were not present.

All of the RCTs have given some details about the expertise/experience of the practitioners and with a well-structured protocol. As the need and significance of this analysis mentioned, the main idea of the conducted researches were to create respectable base for future trial in this field. Since MFR practices vary from clinician to clinician or studies to studies, the authors were recommending more uniformity in the practice.

The analysed systematic review on MFR was published in 2015 and was designed to assess the quality, results and limitations of 19 RCTs found in a multi-database literature search of peer-reviewed articles in the English language based on clear inclusion criteria. AMSTAR 2 was used to measure the quality of the systematic review and demonstrated moderate methodological quality as a whole. Omission of a risk of bias analysis was the major limitation found. Considering the varying quality and standard of the RCTs reviewed, an analysis of the possible biases or flaws might have been an advantage. Lack of heterogeneity testing, missing components in ‘comprehensive research strategy’ and study setting details were the other limitations found but they were justified under limitations of the study. The selected RCTs assessed a total of 1228 patients with the sample sizes varying from 10 to 200 with a mean (SD) of 65 (44) patients. The methodological qualities of the included RCTs were moderate to high. Rating with CEBM Scale revealed that 14 RCTs were in the category of 2b while the remaining were in category 1b. In many of these trials, the MFR treatment was adjunctive to other treatments and the potential specific MFR effect could not be determined. The authors quoted, “MFR may be useful as either a unique therapy or as an adjunct therapy to other established therapies for a variety of conditions”.

In assessing the validity of this systematic review, it had clear inclusion and exclusion criteria and a sensitive search strategy. Included trials were assessed for quality using recognized critical appraisal tools. Overall, this systematic review can be recommended as a starting point for assessing the quality and variety of available evidence on the efficacy of



MFR. Even though the systematic review clearly focuses on Myofascial release, the included studies were very heterogeneous. The reviewer tried to mention such issues like the heterogeneity of the population, treatments applied, outcome measure usage and assessment and the quality of studies included. Though the result of the review was pointing towards advocating its usefulness, there were a number of threats that challenge the statistical inferences underpinning these findings. The main issue was with the generalization of the result. They were even advocating caution on the result interpretation due to the possible type I error resulted from the underpowered samples. This review can only suggest a clinician that there is evidence that MFR alone or added to other conventional therapies, relieves pain and improves function not lesser than conventional therapies studied. Recommendations for future randomised, effectiveness trials on MFRs include: a-priori calculated sample sizes, adequate power, reliable and validated outcome measures, limiting the sources of bias, follow-up time points beyond 24 hours and appropriate levels of significance, assessing threats to statistical validity and appropriate registration. Most importantly, RCTs should present between group differences and desist from reporting within group differences as evidence of effectiveness.

These recommendations would support inferences of clinically meaningful results and facilitate future meta-analyses. This review also supports for the call for transparency within all clinical trials and endorsing of journal adoption of reporting guidelines. The subjective component of MFR must be addressed in future study designs as it is having a major relevance in these types.

This systematic review concludes by stating various measures to be incorporated in the future trials. The authors were optimistic that by adhering to such guidelines in the future will surely result in much higher quality studies there by more accurate results. This analysis supports many of the norms put forward by the systematic review authors and believes that such attempts will make the research in physical therapy field more valid and reliable.

Critical appraisal is an important element of evidence-based medicine to carefully and systematically examine research to judge its trustworthiness, value and relevance in a particular context. An in-depth analysis of the selected RCTs and systematic review was attempted here to find out the strength and weakness with suggestions for future works in this field. This analysis concludes that the three RCTs and the systematic review analysed in this review had the potential to move the Myofascial release research into the next level, though methodological flaws and interpretation biases are evident. These types of attempts should be appreciated and facilitated as this will create reputable backgrounds on which high quality future trials can be built on.

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## Appendices

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- 10.1 Effectiveness of direct vs indirect technique myofascial release in the management of tension-type headache*
- 10.2 Effectiveness of myofascial release in the management of lateral epicondylitis in computer professionals*
- 10.3 Effectiveness of myofascial release in the management of chronic low back pain in nursing professionals*
- 10.4 Effectiveness of myofascial release: systematic review of randomised controlled trials*
- 10.5 AMSTR 2 analysis*
- 10.6 List of individuals participated in the trial and their roles in percentage*